=> d his

(FILE 'HOME' ENTERED AT 22:57:12 ON 18 MAR 2003)

FILE 'AGRICOLA, ALUMINIUM, ANABSTR, APOLLIT, AQUIRE, BABS, BIOCOMMERCE, BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CEN, CERAB, CIN, COMPENDEX, CONFSCI, COPPERLIT, CORROSION, ENCOMPLIT, ENCOMPLIT2, FEDRIP, GENBANK, INSPEC, INSPHYS, INVESTEXT, IPA, ...' ENTERED AT 22:57:30 ON 18 MAR 2003

L1 181622 CYTIDIN? OR URIDIN?
L2 688742 (MITOCHONDRIAL (3A) (DISEAS? OR DYSFUNCTION?)) OR (KEARNS-SAYRE
L3 260 L1 (2S) L2
L4 114 L3 NOT PY>1998
L5 55 DUP REM L4 (59 DUPLICATES REMOVED)

=> d l5 total ibib abs
NO VALID FORMATS ENTERED FOR FILE 'ADISINSIGHT'
In a multifile environment, each file must have at least one valid format requested. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):filedefault

L5 ANSWER 1 OF 55 USPATFULL
AN 1998:22209 USPATFULL
TI Methods and compositions for inhibiting uridine secretion
IN Sommadossi, Jean-Pierre, Birmingham, AL, United States
el Kouni, Mahmoud H., Birmingham, AL, United States
PA The UAB Research Foundation, Birmingham, AL, United States (U.S. corporation)
PI US 5723449 19980303
AI US 1996-589017 19960119 (8)
RLI Continuation of Ser. No. US 1993-106225, filed on 13 Aug 1993, now patented, Pat. No. US 5567689
DT Utility
FS Granted
LN.CNT 742
INCL INCLM: 514/050.000
INCLS: 514/049.000; 514/068.000; 514/218.000; 514/533.000
NCL NCLM: 514/050.000
NCLS: 514/049.000; 514/068.000; 514/218.000; 514/533.000
IC [6]
ICM: A61K031-70
ICS: A61K031-55; C07D241-04; A01N043-62
EXF 514/49; 514/50; 514/68; 514/218; 514/533
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 55 USPATFULL
AN 1998:19708 USPATFULL
TI Enzyme inhibitors, their synthesis, and methods for use
IN el Kouni, Mahmoud H., 4632 Round Forest Dr., Mt. Brook, AL, United States 35213-1832
Naguib, Fardos N. M., 4632 Round Forest Dr., Mt. Brook, AL, United States 35213-1832
Schinazi, Raymond F., 1524 Regency Walk Dr., Decatur, GA, United States 30033
PA el Kouni, Mahmoud H., Mt. Brook, AL, United States (U.S. individual)

Naguib, Fardos N. M., Mt. Brook, AL, United States (U.S. individual)
Schinazi, Raymond F., Atlanta, GA, United States (U.S. individual)
PI US 5721241 19980224
AI US 1995-466470 19950606 (8)
RLI Division of Ser. No. US 1993-146838, filed on 2 Nov 1993, now patented, Pat. No. US 5476855
DT Utility
FS Granted
LN.CNT 1128
INCL INCLM: 514/269.000
INCLS: 514/270.000; 514/274.000; 544/300.000; 544/301.000; 544/302.000; 544/303.000; 544/310.000; 544/311.000; 544/314.000
NCL NCLM: 514/269.000
NCLS: 514/270.000; 514/274.000; 544/300.000; 544/301.000; 544/302.000; 544/303.000; 544/310.000; 544/311.000; 544/314.000
IC [6]
ICM: A61K031-505
ICS: C07D239-02
EXF 544/300; 544/301; 544/302; 544/303; 544/310; 544/311; 544/314; 514/269; 514/270; 514/274
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 55 WPIDS (C) 2003 THOMSON DERWENT
AN 1998-557118 [47] WPIDS
DNN N1998-434279 DNC C1998-166699
TI Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors.
DC B04 D16 S03
IN HANOVER, J A; LUBAS, W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES
CYC 80
PI WO 9844123 A2 19981008 (199847)* EN 56p C12N015-54
RW: AT BE CH DE DK ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9869425 A 19981022 (199910) C12N015-54
ADT WO 9844123 A2 WO 1998-US6101 19980327; AU 9869425 A AU 1998-69425 19980327
FDT AU 9869425 A Based on WO 9844123
PRAI US 1997-42270P 19970331
IC ICM C12N015-54
ICS C12N001-21; C12N005-10; C12N009-10; C12Q001-48; G01N033-50

L5 ANSWER 4 OF 55 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED.
AN 1998-0416002 PASCAL
CP Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.
TIEN Differential chromosome sensitivity to 5-azacytidine in Alzheimer's disease
AU MARQUES PAYAO S. L.; DE ARRUDA CARDOSO SMITH M.; FERREIRA BERTOLUCCI P. H.
CS Departamento de Morfologia, Disciplina de Genetica, Paulista de Medicina, Sao Paulo, Brazil; Departamento de Neurologia Clinica, UNIFESP/Escola Paulista de Medicina, Sao Paulo, Brazil
SO Gerontology : (Basel), (1998), 44(5), 267-271, 31 refs.

ISSN: 0304-324X CODEN: GERNDJ
DT Journal
BL Analytic
CY Switzerland
LA English
AV INIST-8223, 354000072684520030

L5 ANSWER 5 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
AN 1998:28527381 BIOTECHNO
TI Run-on gene transcription in human neocortical nuclei: Inhibition by nanomolar aluminum and implications for neurodegenerative disease
AU Lukiw W.J.; LeBlanc H.J.; Carver L.A.; McLachlan D.R.C.; Bazan N.G.
CS W.J. Lukiw, Louisiana State Univ. Medical Center, Neuroscience Center, Department of Ophthalmology, 2020 Gravier Street, New Orleans, LA 70112, United States.
SO Journal of Molecular Neuroscience, (1998), 11/1 (67-78), 81 reference(s) CODEN: JMNEES ISSN: 0895-8696
DT Journal; Article
CY United States
LA English
SL English

L5 ANSWER 6 OF 55 LIFESCI COPYRIGHT 2003 CSA
AN 2000:9430 LIFESCI
TI RNA editing in plant mitochondria, cytoplasmic male sterility and plant breeding
AU Araya, A.*; Zabaleta, E.; Blanc, V.; Begu, D.; Hernould, M.; Mouras, A.; Litvak, S.
CS Laboratoire REGER. EP 630. CNRS-Universite Victor Segalen Bordeaux 2. 1 rue Camille Saint Saeens. 33077 Bordeaux cedex. France
SO Electronic Journal of Biotechnology [Ejb], (19980415) vol. 1, no. 1, [np]. ISSN: 0717-3458.
DT Journal
TC General Review
FS W2
LA English
SL English

L5 ANSWER 7 OF 55 MEDLINE DUPLICATE 2
AN 1998078289 MEDLINE
DN 98078289 PubMed ID: 9416333
TI Blood-brain barrier disruption, HSP70 expression and apoptosis due to 3-nitropropionic acid, a mitochondrial toxin.
AU Sato S; Gobbel G T; Li Y; Kondo T; Murakami K; Sato M; Hasegawa K; Copin J C; Honkaniemi J; Sharp F R; Chan P H
CS Department of Neurological Surgery, University of California, School of Medicine, San Francisco, USA.
NC AG 08938 (NIA)
NS 14543 (NINDS)
NS 25372 (NINDS)
+
SO ACTA NEUROCHIRURGICA. SUPPLEMENTUM, (1997) 70 237-9.
Journal code: 0140560. ISSN: 0065-1419.
CY Austria
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

EM 199802
ED Entered STN: 19980306
Last Updated on STN: 19980306
Entered Medline: 19980226

L5 ANSWER 8 OF 55 USPATFULL
AN 96:97027 USPATFULL
TI Methods for increasing uridine levels with L-nucleosides
IN Sommadossi, Jean-Pierre, Birmingham, AL, United States
el Kouni, Mahmoud H., Birmingham, AL, United States
PA The UAB Research Foundation, Birmingham, AL, United States (U.S. corporation)
PI US 5567689 19961022
AI US 1993-106225 19930813 (8)
DT Utility
FS Granted
LN.CNT 752
INCL INCLM: 514/050.000
INCLS: 514/049.000; 514/068.000; 514/218.000; 514/533.000
NCL NCLM: 514/050.000
NCLS: 514/049.000; 514/068.000; 514/218.000; 514/533.000
IC [6]
ICM: A61K031-70
ICS: A61K031-55; C07D241-04; A01N043-62
EXF 514/533; 514/183; 514/88; 514/49; 514/50; 514/68; 514/218; 536/28.53
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 9 OF 55 USPATFULL
AN 95:112540 USPATFULL
TI Enzyme inhibitors, their synthesis and methods for use
IN el Kouni, Mahmoud, 4632 Round Forest Dr., Mt. Brook, AL, United States 35213-1832
Naguib, Fardos N. M., 4632 Round Forest Dr., Mt. Brook, AL, United States 35213-1832
Schinazi, Raymond F., 1524 Regency Walk Dr., Decatur, GA, United States 30033
PA el Kouni, Mahmoud H., Mt. Brook, AL, United States (U.S. individual)
Naguib, Fardos N. M., Mt. Brook, AL, United States (U.S. individual)
Schinazi, F., Atlanta, GA, United States (U.S. individual)
PI US 5476855 19951219
AI US 1993-146838 19931102 (8)
DT Utility
FS Granted
LN.CNT 994
INCL INCLM: 514/269.000
INCLS: 514/270.000; 514/274.000; 544/300.000; 544/301.000; 544/302.000; 544/303.000; 544/310.000; 544/311.000; 544/314.000
NCL NCLM: 514/269.000
NCLS: 514/270.000; 514/274.000; 544/300.000; 544/301.000; 544/302.000; 544/303.000; 544/310.000; 544/311.000; 544/314.000
IC [6]
ICM: A61K031-505
ICS: C07D239-02
EXF 544/300; 544/301; 544/302; 544/303; 544/310; 544/311; 544/314; 544/269; 514/269; 514/270; 514/274
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 10 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
AN 1995:25050797 BIOTECHNO
TI Respiratory-deficient human fibroblasts exhibiting defective mitochondrial DNA replication
AU Bodnar A.G.; Cooper J.M.; Leonard J.V.; Schapira H.V.
CS Department of Clinical Neurosciences, Royal Free Hospital School Medicine, University of London,London NW3 2PF, United Kingdom.
SO Biochemical Journal, (1995), 305/3 (817-822)
CODEN: BIJOAK ISSN: 0264-6021
DT Journal; Article
CY United Kingdom
LA English
SL English

L5 ANSWER 11 OF 55 SCISEARCH COPYRIGHT 2003 ISI (R) DUPLICATE 4
AN 95:104003 SCISEARCH
GA The Genuine Article (R) Number: QD409
TI METABOLISM AND ACTIONS OF CDP-CHOLINE AS AN ENDOGENOUS COMPOUND AND ADMINISTERED EXOGENOUSLY AS CITICOLINE
AU WEISS G B (Reprint)
CS M HURLEY & ASSOCIATES INC, 571 CENT AVE, MURRAY HILL, NJ, 07974 (Reprint)
CYA USA
SO LIFE SCIENCES, (20 JAN 1995) Vol. 56, No. 9, pp. 637-660.
ISSN: 0024-3205.
DT General Review; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 184
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L5 ANSWER 12 OF 55 ADISCTI COPYRIGHT 2003 (ADIS)
AN 1995:38451 ADISCTI
DN 800378614
TI Posatirelin for the treatment of late-onset Alzheimer's disease: a double-blind multicentre study vs citicoline and ascorbic acid.
ADIS TITLE: Posatirelin vs citicoline: therapeutic use.
Alzheimer's disease.
AU Parnetti L; Ambrosoli L; Abate G; Azzini C; Balestreri R; et al.
CS Perugia University, Perugia, Italy; Poli Industria Chimica S.p.A., Milan, Italy.
SO Acta Neurologica Scandinavica (Aug 1, 1995), Vol. 92, pp. 135-140
DT Study
RE Alzheimer's Disease and Cognition Disorders
FS Summary
LA English
WC 718

L5 ANSWER 13 OF 55 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED. DUPLICATE
AN 1996-0052512 PASCAL
CP Copyright .COPYRGT. 1996 INIST-CNRS. All rights reserved.
TIEN CDP-choline : pharmacological and clinical review
AU SECADES J. J.; FRONTERA G.
CS FISA medical dep., Barcelona, Spain
SO Methods and findings in experimental and clinical pharmacology, (1995), 17(SUPB), 1-54, 239 refs.
ISSN: 0379-0355

DT Journal
BL Analytic
CY Spain
LA English
AV INIST-18217, 354000054975660010

L5 ANSWER 14 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1996:466219 BIOSIS
DN PREV199699188575
TI Multi-infarct dementia: Modification of the P300 cognitive event-related potential in patients treated with the association of cytidine and uridine.
AU Gallai, V.; Alberti, A.; Mazzotta, G.
CS Clin. Neurol., Univ. degli Studi, Perugia Italy
SO Rivista di Neuropsichiatria e Scienze Affini, (1995) Vol. 41, No. 1, pp. 1-9.
ISSN: 0035-6352.
DT Article
LA Italian
SL Italian; English

L5 ANSWER 15 OF 55 SCISEARCH COPYRIGHT 2003 ISI (R)
AN 94:716280 SCISEARCH
GA The Genuine Article (R) Number: PQ346
TI AMYLOID PRECURSOR PROTEIN MESSENGER-RNA STABILITY IS CONTROLLED BY A 29-BASE ELEMENT IN THE 3'-UNTRANSLATED REGION
AU ZAIDI S H E; MALTER J S (Reprint)
CS UNIV WISCONSIN HOSP & CLIN, DEPT PATHOL & LAB MED, A4-204-CSC, 600 HIGHLAND AVE, MADISON, WI, 53792 (Reprint); UNIV WISCONSIN, DEPT PATHOL & LAB MED, NEUROSCI PROGRAM, MADISON, WI, 53792; UNIV WISCONSIN, INST AGING, MADISON, WI, 53792
CYA USA
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (30 SEP 1994) Vol. 269, No. 39, pp. 24007-24013.
ISSN: 0021-9258.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L5 ANSWER 16 OF 55 SCISEARCH COPYRIGHT 2003 ISI (R)
AN 94:716279 SCISEARCH
GA The Genuine Article (R) Number: PQ346
TI MULTIPLE PROTEINS INTERACT AT A UNIQUE CIS-ELEMENT IN THE 3'-UNTRANSLATED REGION OF AMYLOID PRECURSOR PROTEIN MESSENGER-RNA
AU ZAIDI S H E; DENMAN R; MALTER J S (Reprint)
CS UNIV WISCONSIN HOSP & CLIN, DEPT PATHOL & LAB MED, A4-204-CSC, 600 HIGHLAND AVE, MADISON, WI, 53792 (Reprint); UNIV WISCONSIN, DEPT PATHOL & LAB MED, NEUROSCI PROGRAM, MADISON, WI, 53792; UNIV WISCONSIN, INST AGING, MADISON, WI, 53792; NEW YORK STATE INST BASIC RES DEV DISABIL, STATEN ISL, NY, 10314
CYA USA
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (30 SEP 1994) Vol. 269, No. 39, pp. 24000-24006.
ISSN: 0021-9258.
DT Article; Journal

FS LIFE
LA ENGLISH
REC Reference Count: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L5 ANSWER 17 OF 55 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED. DUPLICATE
AN 1995-0163958 PASCAL
CP Copyright .COPYRGT. 1995 INIST-CNRS. All rights reserved.
TIEN Brain mapping activity and mental performance after chronic treatment with CDP-choline in Alzheimer's disease
AU FRANCO-MAŞIDE A.; CAAMANO J.; GOMEZ M. J.; CACABELOS R.
CS Inst. cent. nervous system disorders, basic clin. neuros. res. cent., dep. digital diagnosis clin. neurosci., 15080 La Coruna, Spain
SO Methods and findings in experimental and clinical pharmacology, (1994), 16(8), 597-607, 45 refs.
ISSN: 0379-0355
DT Journal
BL Analytic
CY Spain
LA English
AV INIST-18217, 354000057830070070

L5 ANSWER 18 OF 55 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED. DUPLICATE
AN 1994-0437018 PASCAL
CP Copyright .COPYRGT. 1994 INIST-CNRS. All rights reserved.
TIEN CDP-choline-induced blood histamine changes in Alzheimer's disease
AU FERNANDEZ-NOVOA L.; ALVAREZ X. A.; FRANCO-MASIDE A.; CAAMANO J.; CACABELOS R.
CS Complutense univ. medical school, dep. human physiology, neurogerontology unit, 28040 Madrid, Spain
SO Methods and findings in experimental and clinical pharmacology, (1994), 16(4), 279-284, 38 refs.
ISSN: 0379-0355
DT Journal
BL Analytic
CY Spain
LA English
AV INIST-18217, 354000045285930070

L5 ANSWER 19 OF 55 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 8
AN 1994:548887 CAPLUS
DN 121:148887
TI Effects of CDP-choline on cognition and cerebral hemodynamics in patients with Alzheimer's disease
AU Caamano, J.; Gomez, M.J.; Franco, A.; Cacabelos, R.
CS Basic Clin. Neurosci. Res. Cent., Inst. C.N.S. Dis., La Coruna, Spain
SO Methods and Findings in Experimental and Clinical Pharmacology (1994), 16(3), 211-18
CODEN: MFEPDX; ISSN: 0379-0355
DT Journal
LA English

L5 ANSWER 20 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
AN 1994:24023911 BIOTECHNO
TI Enzymatic amplification of synthetic oligodeoxyribonucleotides:

Implications for triplet repeat expansions in the human genome
AU Behn-Krappa A.; Doerfler W.
CS Institute of Genetics, University of Cologne,D-50931 Cologne, Germany.
SO Human Mutation, (1994), 3/1 (19-24)
CODEN: HUMUE3 ISSN: 1059-7794
DT Journal; Article
CY United States
LA English
SL English

L5 ANSWER 21 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
AN 1993:23304139 BIOTECHNO
TI Nuclear complementation restores mtDNA levels in cultured cells from a patient with mtDNA depletion
AU Bodnar A.G.; Cooper J.M.; Holt I.J.; Leonard J.V.; Schapira A.H.V.
CS Department of Neurological Science, Royal Free Hospital Sch. of Medicine, Rowland Hill Street,London NW3 2PF, United Kingdom.
SO American Journal of Human Genetics, (1993), 53/3 (663-669)
CODEN: AJHGAG ISSN: 0002-9297
DT Journal; Article
CY United States
LA English
SL English

L5 ANSWER 22 OF 55 CAPLUS COPYRIGHT 2003 ACS
AN 1993:166580 CAPLUS
DN 118:166580
TI RNA metabolism in human brain during aging and in Alzheimer's disease. RNA synthesis in the nuclei isolated from postmortem brain tissue
AU Sajdel-Sulkowska, Elizabeth M.
CS Neurobiol. Lab., Massachusetts Gen. Hosp., Boston, MA, USA
SO Advances in Behavioral Biology (1992), 40(Treat. Dementias), 397-406
CODEN: ADBBBW; ISSN: 0099-6246
DT Journal
LA English

L5 ANSWER 23 OF 55 DRUGU COPYRIGHT 2003 THOMSON DERWENT
AN 1992-46037 DRUGU P
TI Medicinal Benefits of the Mushroom Ganoderma.
AU Jong S C; Birmingham J M
LO Rockville, Maryland, United States
SO Adv.Appl.Microbiol. (37, 101-34, 1992) 11 Fig. 1 Tab. 142 Ref.
CODEN: ADAMAP ISSN: 0065-2164
AV Mycology and Botany Department, American Type Culture Collection, Rockville, Maryland 20852, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature

L5 ANSWER 24 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1992:491437 BIOSIS
DN BR43:100637
TI THE EXPRESSION OF THE AMYLOID PRECURSOR PROTEIN APP IS REGULATED BY TWO GC-ELEMENTS IN THE PROMOTER.
AU POLLWEIN P; POLLWEIN R; MASTERS C L; BEYREUTHER K
CS CENT. MOL. BIOL. HEIDELBERG, UNIV. HEIDELBERG, D-6900 HEIDELBERG, GER.

SO THIRD INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED DISORDERS, ABANO TERME, ITALY, JULY 12-17, 1992. NEUROBIOL AGING. (1992) 13 (SUPPL 1), S71-S72.
CODEN: NEAGDO. ISSN: 0197-4580.
DT Conference
FS BR; OLD
LA English

L5 ANSWER 25 OF 55 SCISEARCH COPYRIGHT 2003 ISI (R) DUPLICATE 11
AN 91:204210 SCISEARCH
GA The Genuine Article (R) Number: FE557
TI AN RNA CODING FOR THE **ALZHEIMER** AMYLOID PRECURSOR PROTEIN INTERACTS INVITRO WITH THE ADENOSINE-**URIDINE** BINDING-FACTOR
AU MALTER J (Reprint); MILLER D L; DENMAN R
CS TULANE UNIV, SCH MED, DEPT PATHOL, NEW ORLEANS, LA, 70112; NEW YORK STATE INST BASIC RES DEV DISABILITIES, STATEN ISL, NY, 10314
CYA USA
SO FASEB JOURNAL, (1991) Vol. 5, No. 6, pp. A1606.
DT Conference; Journal
FS LIFE
LA ENGLISH
REC No References

L5 ANSWER 26 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1990:120063 BIOSIS
DN BR38:54273
TI CHOLINE METABOLISM IN CHOLINERGIC NEURONS IMPLICATIONS FOR THE PATHOGENESIS OF NEURODEGENERATIVE DISEASES.
AU WURTMAN R J; KRZYSZTOF BLUSZTAJN J; ULUS I H; G-COVIELLA I L; BUYUKUYSAL R L; GROWDON J H; SLACK B E
CS DEP. BRAIN COGNITIVE SCI., MASS. INST. TECHNOL., CAMBRIDGE, MASS. 02139.
SO WURTMAN, R. J., ET AL. (ED.). ADVANCES IN NEUROLOGY, VOL. 51. ALZHEIMER'S DISEASE. XXVII+282P. RAVEN PRESS: NEW YORK, NEW YORK, USA. ILLUS. (1990) 0 (0), 117-126.
CODEN: ADNRA3. ISSN: 0091-3952. ISBN: 0-88167-574-1.
FS BR; OLD
LA English

L5 ANSWER 27 OF 55 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 12
AN 1989:470975 CAPLUS
DN 111:70975
TI Phosphoethanolamine for treatment of Alzheimer's disease
IN Appel, Stanley H.
PA Baylor College of Medicine, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8809171	A1	19881201	WO 1988-US1693	19880518
	W: AU, DK, JP				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8817909	A1	19881221	AU 1988-17909	19880518
PRAI	US 1987-51897		19870519		
	US 1988-188005		19880511		

WO 1988-US1693 19880518
OS MARPAT 111:70975

L5 ANSWER 28 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 13
AN 1988:355300 BIOSIS
DN BA86:50778
TI PHOSPHORUS-31 NMR STUDY OF THE BRAIN IN ALZHEIMER'S DISEASE.
AU PETTEGREW J W; MOOSSY J; WITHERS G; MCKEAG D; PANCHALINGAM K
CS LAB. NEUROPHYSICS, DEP. PSYCHIATRY AND NEUROL., UNIV. PITTSBURGH, WESTERN PSYCHIATRIC INST. AND CLINIC, 3811 O'HARA ST., PITTSBURGH, PA. 15213.
SO J NEUROPATHOL EXP NEUROL, (1988) 47 (3), 235-248.
CODEN: JNENAD. ISSN: 0022-3069.
FS BA; OLD
LA English

L5 ANSWER 29 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1988:170565 BIOSIS
DN BR34:85177
TI RADIOACTIVE **URIDINE** INCORPORATION INTO RNA BY POSTMORTEM HUMAN BRAIN TISSUE EVIDENCE FOR POSTMORTEM TRANSCRIPTION IN THE **ALZHEIMER** BRAIN.
AU SAJDEL-SULKOWSKA E M; MAROTTA C A
CS DEP. PSYCHIATRY, HARVARD MED. SCH., BELMONT, MA 02178, USA.
SO 17TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, NEW ORLEANS, LOUISIANA, USA, NOVEMBER 16-21, 1987. SOC NEUROSCI ABSTR. (1987) 13 (2), 1326.
CODEN: ASNEE5.
DT Conference
FS BR; OLD
LA English

L5 ANSWER 30 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
AN 1986:16049347 BIOTECHNO
TI Intravenous uridine treatment antagonizes hypoglycaemia-induced reduction in brain somatostatin-like immunoreactivity
AU Agnati L.F.; Fuxe K.; Eneroth P.; et al.
CS Department of Human Physiology, University of Modena, Modena, Italy.
SO Acta Physiologica Scandinavica, (1986), 126/4 (525-531)
CODEN: APSCAX
DT Journal; Article
CY Sweden
LA English

L5 ANSWER 31 OF 55 WPIDS (C) 2003 THOMSON DERWENT
AN 1984-290125 [47] WPIDS
DNC C1984-123174
TI Compsn. containing amino acid and choline or precursor - useful for treating neurological disease or ageing.
DC B05
IN WURTMAN, R J
PA (MASI) MASSACHUSETTS INST TECHNOLOGY
CYC 16
PI EP 125900 A 19841121 (198447)* EN 20p
R: AT BE CH DE FR GB IT LI LU NL SE
JP 60214734 A 19851028 (198549)
ES 8602409 A 19860316 (198620)

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     US 4624852    A  19861125 (198650)
     CA 1228301    A  19871020 (198746)
     IL 71819      A  19871231 (198809)
     US 4737489    A  19880412 (198817)
     US 4775665    A  19881004 (198842)
     EP 125900     B  19890823 (198934)  EN
         R: AT BE CH DE FR GB IT LI LU NL SE
     JP 01041124   B  19890904 (198939)
     DE 3479477    G  19890928 (198940)
ADT  EP 125900 A EP 1984-303195 19840511; JP 60214734 A JP 1984-94739 19840514;
     ES 8602409 A ES 1984-532873 19840515; US 4624852 A US 1984-613000
     19840521; US 4737489 A US 1984-685591 19841221; US 4775665 A US
     1987-102062 19870924
PRAI US 1983-495202   19830516; US 1984-613000   19840521; US 1984-685591
     19841221; US 1987-102062   19870924
IC   A61K031-19; C07C091-26; C07C101-04; C07D209-18

L5   ANSWER 32 OF 55  WPIDS (C) 2003 THOMSON DERWENT
AN   1984-244938 [40]   WPIDS
DNC  C1984-103379
TI   Treating disturbances of central and peripheral nervous systems - with
     cytidine mono phosphate of galactono-nulosaminic acid derivative.
DC   B03
IN   DECORTE, E; MICCOLI, P
PA   (CRCH) CRC CIA DI RICERCHE CHIM SA
CYC  14
PI   EP 120328     A  19841003 (198440)* EN   26p
         R: AT BE CH DE FR GB LI LU NL SE
     JP 60006618   A  19850114 (198508)
     CA 1219539    A  19870324 (198716)
     US 4704361    A  19871103 (198746)
     EP 120328     B  19881019 (198842)# EN
         R: AT BE CH DE FR GB LI LU NL SE
     CA 1243971    A  19881101 (198848)
     DE 3474632    G  19881124 (198848)
     JP 02016732   B  19900418 (199019)
     IT 1175061    B  19870701 (199029)#
     IT 1175084    B  19870701 (199029)
     US 5070079    A  19911203 (199151)
ADT  EP 120328 A EP 1984-102059 19840228; JP 60006618 A JP 1984-36341 19840229;
     US 4704361 A US 1984-584805 19840229; JP 02016732 B JP 1984-36341
     19840229; US 5070079 A US 1990-560239 19900723
PRAI IT 1983-83371    19830420; IT 1983-34183    19830301; IT 1983-83341
     19830301
IC   A61K031-70; C07H013-04; C07H019-10; C12N009-96; C12N011-10; C12P019-26;
     C12R001-19

L5    ANSWER 33 OF 55  DRUGU  COPYRIGHT 2003 THOMSON DERWENT
AN    1983-44742  DRUGU   M B
TI    Antiviral Response of Fibroblasts from Familial Alzheimer's Disease and
      Down's Syndrome to Human Interferon-Alpha.
AU    Mowshowitz S L; Dawson G J; Elizan T S
LO    New York, New York, United States
SO    J.Neural Transm. (57, No. 1-2, 121-26, 1983) 1 Tab. 15 Ref.
      CODEN: JNTMAH       ISSN:  0300-9564
AV    Departments of Microbiology and Neurology, The Mount Sinai School of
      Medicine of the City University of New York, New York, N.Y., U.S.A.
```

LA English
DT Journal
FA AB; LA; CT
FS Literature

L5 ANSWER 34 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.
AN 1981:11090125 BIOTECHNO
TI Differential labelling of UDP-N-acetylglucosamine in Huntington's-chorea fibroblasts
AU Hung W.Y.; Tourian A.
CS Neurogenet. Cell Biol. Lab., Div. Neurol., Dept. Med., Duke Univ. Med Cent., Durham, N.C. 27710, United States.
SO Biochemical Journal, (1981), 196/2 (495-498)
CODEN: BIJOAK
DT Journal; Article
CY United Kingdom
LA English

L5 ANSWER 35 OF 55 FEDRIP COPYRIGHT 2003 NTIS
AN 2003:184933 FEDRIP
NR CRISP 5R01MH28783-25
TI PSYCHOPHARMACOLOGICAL EFFECTS OF EXOGENOUS CHOLINE
SF Principal Investigator: WURTMAN, RICHARD J; MASSACHUSETTS INST OF TECH, 77 MASSACHUSETTS AVE, CAMBRIDGE, MA 02139
CSP MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, MASSACHUSETTS
CSS Supported By: NATIONAL INSTITUTE OF MENTAL HEALTH
FYR 2001
FU Noncompeting Continuation (Type 5)
FS National Institutes of Health

L5 ANSWER 36 OF 55 INVESTEXT COPYRIGHT 2003 TFS

AN 1999:090791 INVESTEXT(tm) REPORT NUMBER:3367196
PGNO PAGE 21 OF 33
DN 3367196
TI Swiss Pharmaceuticals
AU Kulhoff, B.
CS BANK SARASIN & CO.; SWITZERLAND
CSR WESTERN EUROPE REGION; EUROPE
CSTY Financial center investment bank-broker
PD 1 Sep 1998
DT INDUSTRY REPORT
FS Text Page; INDUSTRY REPORT
WC 248

L5 ANSWER 37 OF 55 INVESTEXT COPYRIGHT 2003 TFS

AN 1998:199451 INVESTEXT(tm) REPORT NUMBER:2600717
PGNO PAGE 7 OF 17
DN 2600717
TI Roche - Company Report
AU Hauber, A., et al
CS SALOMON BROTHERS INC.; NEW YORK (STATE OF)
CSR MID-ATLANTIC/MIDDLE ATLANTIC REGION; UNITED STATES OF AMERICA; NORTH AMERICA
CSTY Financial center investment bank-broker
PD 30 Oct 1997

DT COMPANY REPORT
FS Text Page; COMPANY REPORT
WC 189

L5 ANSWER 38 OF 55 INVESTEXT COPYRIGHT 2003 TFS

AN 94:741646 INVESTEXT(tm) REPORT NUMBER:1464711
PGNO PAGE 15 OF 57
DN 1464711
TI Biotechnology April 1994 Performance - Industry Report
AU Miller, L.I., et al
CS PAINEWEBBER INC.; NEW YORK (STATE OF)
CSR MID-ATLANTIC/MIDDLE ATLANTIC REGION; UNITED STATES OF AMERICA; NORTH AMERICA
CSTY Financial center investment bank-broker
PD 19 May 1994
DT INDUSTRY REPORT
FS Text Page; INDUSTRY REPORT
WC 460

L5 ANSWER 39 OF 55 ADISINSIGHT COPYRIGHT 2003 (ADIS)
ACCESSION NUMBER: 2003:119 ADISINSIGHT
SOURCE: Adis R&D Insight
DOCUMENT NO: 018357
CHANGE DATE: Feb 17, 2003
GENERIC NAME: RG 2133
SYNONYM: RG2133; Tracetyluridine - Repligen; Uridine prodrug
MOLECULAR FORMULA:Unspecified
STRUCTURE:
STRUCTURE DIAGRAM IS NOT AVAILABLE

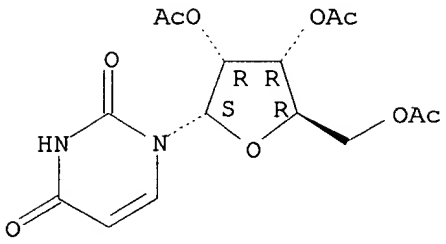
EPHMRA ATC CODE: A16A Other Alimentary Tract and Metabolism Products; N6A Anti-Depressants
WHO ATC CODE: A16A Other Alimentary Tract and Metabolism Products; N06A Antidepressants
HIGHEST DEV. PHASE: Phase I

COMPANY INFORMATION
ORIGINATOR: Repligen (United States)
PARENT: Repligen

WORD COUNT: 131

L5 ANSWER 40 OF 55 ADISINSIGHT COPYRIGHT 2003 (ADIS)
ACCESSION NUMBER: 1998:4716 ADISINSIGHT
SOURCE: Adis R&D Insight
DOCUMENT NO: 005276
CHANGE DATE: Jan 31, 2003
GENERIC NAME: Triacetyluridine
SYNONYM: PN 401; PN401; TAU
CHEMICAL NAME: 2,4(1H,3H)-Pyrimidinedione, 1-(2,3,5-tri-O-acetyl-alpha-D-ribofuranosyl)-
MOLECULAR FORMULA: C15 H18 N2 O9
CAS REGISTRY NO.: 59279-50-4
STRUCTURE:

Absolute stereochemistry.



EPHMRA ATC CODE: A10X Other Drugs Used in Diabetes; N4 Anti-Parkinson Drugs; N7X All other CNS drugs
WHO ATC CODE: A10X Other Drugs Used in Diabetes; N04 Anti-Parkinson Drugs; N07X Other Nervous System Drugs
HIGHEST DEV. PHASE: Phase III

COMPANY INFORMATION
ORIGINATOR: Wellstat Therapeutics Corporation (United States)
PARENT: Wellstat Therapeutics Corporation

WORD COUNT: 368

L5 ANSWER 41 OF 55 DGENE (C) 2003 THOMSON DERWENT
AN AAW82500 Protein DGENE
TI Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
IN Hanover J A; Lubas W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
PI WO 9844123 A2 19981008 56p
AI WO 1998-US6101 19980327
PRAI US 1997-42270 19970331
DT Patent
LA English
OS 1998-557118 [47]

L5 ANSWER 42 OF 55 DGENE (C) 2003 THOMSON DERWENT
AN AAW82503 Protein DGENE
TI Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
IN Hanover J A; Lubas W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
PI WO 9844123 A2 19981008 56p
AI WO 1998-US6101 19980327
PRAI US 1997-42270 19970331
DT Patent
LA English
OS 1998-557118 [47]

L5 ANSWER 43 OF 55 DGENE (C) 2003 THOMSON DERWENT
AN AAW82502 Protein DGENE
TI Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors

IN Hanover J A; Lubas W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
PI WO 9844123 A2 19981008 56p
AI WO 1998-US6101 19980327
PRAI US 1997-42270 19970331
DT Patent
LA English
OS 1998-557118 [47]

L5 ANSWER 44 OF 55 DGENE (C) 2003 THOMSON DERWENT
AN AAW82501 Protein DGENE
TI Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
IN Hanover J A; Lubas W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
PI WO 9844123 A2 19981008 56p
AI WO 1998-US6101 19980327
PRAI US 1997-42270 19970331
DT Patent
LA English
OS 1998-557118 [47]

L5 ANSWER 45 OF 55 DGENE (C) 2003 THOMSON DERWENT
AN AAR79354 Protein DGENE
TI Human double stranded ribonucleotide acid adenosine deaminase enzyme, DRADA - useful in treating neuro-degenerative disorder(s) e.g. Alzheimer's disease, etc.
IN Nishikura K
PA (WIST-N) WISTAR INST ANATOMY & BIOLOGY.
PI WO 9522604 A1 19950824 98p
AI WO 1995-US2275 19950216
PRAI US 1994-280443 19940725
US 1994-197794 19940217
DT Patent
LA English
OS 1995-302713 [39]

L5 ANSWER 46 OF 55 DGENE (C) 2003 THOMSON DERWENT
AN AAV69303 DNA DGENE
TI Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
IN Hanover J A; Lubas W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
PI WO 9844123 A2 19981008 56p
AI WO 1998-US6101 19980327
PRAI US 1997-42270 19970331
DT Patent
LA English
OS 1998-557118 [47]

L5 ANSWER 47 OF 55 DGENE (C) 2003 THOMSON DERWENT
AN AAV69304 DNA DGENE
TI Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors

IN Hanover J A; Lubas W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
PI WO 9844123 A2 19981008 56p
AI WO 1998-US6101 19980327
PRAI US 1997-42270 19970331
DT Patent
LA English
OS 1998-557118 [47]

L5 ANSWER 48 OF 55 DGENE (C) 2003 THOMSON DERWENT
AN AAV69301 DNA DGENE
TI Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
IN Hanover J A; Lubas W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
PI WO 9844123 A2 19981008 56p
AI WO 1998-US6101 19980327
PRAI US 1997-42270 19970331
DT Patent
LA English
OS 1998-557118 [47]

L5 ANSWER 49 OF 55 DGENE (C) 2003 THOMSON DERWENT
AN AAV69306 DNA DGENE
TI Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
IN Hanover J A; Lubas W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
PI WO 9844123 A2 19981008 56p
AI WO 1998-US6101 19980327
PRAI US 1997-42270 19970331
DT Patent
LA English
OS 1998-557118 [47]

L5 ANSWER 50 OF 55 DGENE (C) 2003 THOMSON DERWENT
AN AAV69305 DNA DGENE
TI Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
IN Hanover J A; Lubas W
PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
PI WO 9844123 A2 19981008 56p
AI WO 1998-US6101 19980327
PRAI US 1997-42270 19970331
DT Patent
LA English
OS 1998-557118 [47]

L5 ANSWER 51 OF 55 DGENE (C) 2003 THOMSON DERWENT
AN AAV69302 DNA DGENE
TI Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
IN Hanover J A; Lubas W

PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
PI WO 9844123 A2 19981008 56p
AI WO 1998-US6101 19980327
PRAI US 1997-42270 19970331
DT Patent
LA English
OS 1998-557118 [47]

L5 ANSWER 52 OF 55 PHAR COPYRIGHT 2003 PJB
AN 30768 PHAR
DN 035166
CN triacetyluridine, Wellstat
CN uridine, Wellstat
CN PN-401
CN TAU, Wellstat
STA Active

CO

Type	Company Name (Country)	Development Status
Originator	Wellstat (United States)	Phase III Clinical Trial

SO Pharmaprojects. PJB Publications Ltd., Richmond, Surrey, UK
TX Wellstat Therapeutics (Wellstat) is developing triacetyluridine (PN-401), a po prodrug of the nucleoside, **uridine**, to enable higher dosage of 5-FU to be administered to cancer patients. It is also under development for the treatment of various neurodegenerative disorders associated with **mitochondrial dysfunction**. Its mechanism of action is unknown.

Clinical

Phase IIIIt is in a randomized, open-label Phase III trial in N America in 260 stage II-IV pancreatic cancer patients. Patients will receive PN-401 po once-daily x2 days in combination with either 5-FU iv 1x/wk x3 with 1wk rest for a 4wk cycle or gemcitabine hydrochloride (qv) iv 1x/wk x7 with 1wk rest for a 4wk cycle.

Phase IIIt is in a Phase II trial (S9915) in combination with 5-FU and leucovorin in unresectable or metastatic adenocarcinoma of the stomach.

Phase IIt is in Phase I trials for the treatment of colorectal cancer and neurodegenerative diseases (Company Web Page, Wellstat, Nov 2002).

Preclinical
It has shown efficacy in murine models of Alzheimer's, Huntington's and Parkinson's diseases and in models of peripheral neuropathy. PN-401 was neuroprotective against chemically-induced hypoxia and H2O2 toxicity (32nd Meet Soc Neurosci (Orlando), 2002, Abs 322.4 and 685.15). Entered by KK on 12/11/2002.
DSTA World: Phase III Clinical Trial
Canada: Phase III Clinical Trial
United States: Phase III Clinical Trial

CC K5A Radio-chemosensitizer
N11Z Neurological
N4A Antiparkinsonian
N6D Memory enhancer
N7C Neuroprotective
CT Indication: Cancer, pancreatic; Cancer, stomach; Cancer, colorectal
ORGM CH-SY (Chemical synthesis, synthetic)
RTE A-PO (Alimentary, po)
RDAT 20021112 RNTE ##Act##New Product
PHCD UN; Unidentified pharmacological activity; UN.
PHCD UN.

LN

Therapy (CC)	Pharmacology (PHCD)	Status (DSTC)
K5A	UN	C3
N11Z	UN	C1
N4A	UN	P
N6D	UN	P
N7C	UN	P

LCDAT 20021112: KK : New product entry

STRUCTURE DIAGRAM IS NOT AVAILABLE

L5 ANSWER 53 OF 55 PHAR COPYRIGHT 2003 PJB
AN 27252 PHAR
DN 031648
CN triacetyluridine, RepliGen
CN uridine prodrug, RepliGen
CN TAU, RepliGen
CN RG-2133
STA Active

CO

Type	Company Name (Country)	Development Status
Originator	RepliGen (United States)	Phase II Clinical Trial

SO Pharmaprojects. PJB Publications Ltd., Richmond, Surrey, UK
TX Triacetyluridine (RG-2133) is a prodrug of **uridine** under development by RepliGen for the treatment of bipolar disorder, major depression, renal tubular acidosis and **mitochondrial disease**.

Marketing
RepliGen has licensed from the University of California, San Diego (UCSD), CA, the US, 2 patents covering the use of **uridine** for the treatment of **mitochondrial diseases** and purine autism. RepliGen has exclusive commerical rights in exchange for upfront, milestone and royalty payments (Press releases, RepliGen, 5 Mar 2001 and 23 Jan 2003; Ann Rep, RepliGen, 2002). It has US orphan drug status for use in **mitochondrial**

disease.

Clinical

Phase IIIt is in a 4wk dose-escalation, open-label US Phase I/II trial in 12 patients with mitochondrial disease. RG-2133 tolerance will be evaluated, as well as its impact on symptoms including renal function, seizures or cardiac function (Press release, RepliGen, 13 Feb 2003). An open-label US Phase I/II safety and efficacy trial has also been initiated. The trial will assess the impact of RG-2133 on depressive symptoms, and will evaluate potential changes in brain chemistry by magnetic resonance spectroscopy in 20 patients before and after 6wk of treatment with RG-2133 po (Press release, RepliGen, 23 Jan 2003).

Phase IIn a Phase I trial in 15 **mitochondrial disease** patients (including children), **uridine** po or TAU produced improvements in cognitive and muscular function over 2yr, and was well tolerated (Press release, RepliGen, 14 Dec 2000; Ann Rep, RepliGen, 2002). In 4 patients with renal tubular acidosis, **uridine** or TAU produced a rapid improvement or correction of kidney function (Press release, RepliGen, 5 Mar 2001).

Preclinical
Uridine was active in a well-validated animal model of depression (Press release, RepliGen, 23 Jan 2003). Updated by WB on 17/2/2003.

```
DSTA World: Phase II Clinical Trial
     United States: Phase II Clinical Trial
CC   N10A      Antidepressant
     A17       Metabolic and enzyme disorders
     G4Z       Urological
CT   Indication: Depression, general; Mitochondrial disease; Acidosis
ORGM CH-SY (Chemical synthesis, synthetic)
RTE  A-PO (Alimentary, po)
RDAT 20001220    RNTE ##Act##New Product
     20010305       ##Est##New Therapeutic Activity Urological (G4Z)
     20010305       ##Est##New Indication Acidosis
     20030213       ##Act##Orphan Drug Status Granted The US, Mitochondrial
                      disease
PHCD UN; Unidentified pharmacological activity; UN.
PHCD UN.

LN
Therapy (CC)|Pharmacology (PHCD) |Status (DSTC)
============+====================+============
N10A        |UN                  |C2
------------+--------------------+------------
A17         |UN                  |C2
------------+--------------------+------------
G4Z         |UN                  |C1

NRAT 0:Novelty Rating - Not available
MRAT 5:Market Rating - Over US$ 10000 million
SRAT 3:Speed Rating - Average
TRAT 0:Total Rating - Total Rating unavailable
LCDAT 20030217: WB : Orphan drug status and initiation of Phase I/II trial for
```

mitochondrial disease reported

STRUCTURE DIAGRAM IS NOT AVAILABLE

L5 ANSWER 54 OF 55 BABS COPYRIGHT 2003 BEILSTEIN CDS MDLI
AN 6178733 BABS
TI Metabolism and Actions of CDP-Choline as an Endogenous Compound and Administered Exogenously as Citicoline
AU Weiss, George B.
SO Life Sci. (1995), 56(9), 637 - 660
CODEN: LIFSAK
DT Journal
LA English
SL English

L5 ANSWER 55 OF 55 CONFSCI COPYRIGHT 2003 CSA
AN 91:28743 CONFSCI
DN 91057540
TI RNA coding for the **Alzheimer** amyloid precursor protein interacts in vitro with the adenosine-**uridine** binding factor
AU Malter, J.; Miller, D.L.; Denman, R.
CS Tulane Univ. Sch. Med.
SO FASEB, 9650 Rockville Pike, Bethesda, MD 20814, USA, Abstracts, FASEB Journal.
Meeting Info.: 912 0204: 75th Annual Meeting of FASEB (9120204). Atlanta, GA (USA). 21-25 Apr 1991. Federation of American Societies for Experimental Biology.
DT Conference
FS DCCP
LA UNAVAILABLE

L5 ANSWER 1 OF 55 USPATFULL

ACCESSION NUMBER:	1998:22209 USPATFULL
TITLE:	Methods and compositions for inhibiting uridine secretion
INVENTOR(S):	Sommadossi, Jean-Pierre, Birmingham, AL, United States el Kouni, Mahmoud H., Birmingham, AL, United States
PATENT ASSIGNEE(S):	The UAB Research Foundation, Birmingham, AL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5723449		19980303
APPLICATION INFO.:	US 1996-589017		19960119 (8)

RELATED APPLN. INFO.:	Continuation of Ser. No. US 1993-106225, filed on 13 Aug 1993, now patented, Pat. No. US 5567689
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Kunz, Gary L.
LEGAL REPRESENTATIVE:	Nutter, McClennen & Fish, LLP
NUMBER OF CLAIMS:	13
EXEMPLARY CLAIM:	1
LINE COUNT:	742

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and pharmaceutical compositions effective to increase intracellular and plasma uridine concentrations are disclosed. Certain compositions and methods of using such compositions have been found to be effective to inhibit uridine secretion in a subject, thus increasing uridine concentration. Treatments that increase uridine concentrations are useful to combat many treatments and can also be effective in protecting or rescuing uninfected and normal cells that are subject to toxic side effects induced by the administration of certain chemotherapeutic compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 55 USPATFULL

ACCESSION NUMBER:	1998:19708 USPATFULL
TITLE:	Enzyme inhibitors, their synthesis, and methods for use
INVENTOR(S):	el Kouni, Mahmoud H., 4632 Round Forest Dr., Mt. Brook, AL, United States 35213-1832 Naguib, Fardos N. M., 4632 Round Forest Dr., Mt. Brook, AL, United States 35213-1832 Schinazi, Raymond F., 1524 Regency Walk Dr., Decatur, GA, United States 30033
PATENT ASSIGNEE(S):	el Kouni, Mahmoud H., Mt. Brook, AL, United States (U.S. individual) Naguib, Fardos N. M., Mt. Brook, AL, United States (U.S. individual) Schinazi, Raymond F., Atlanta, GA, United States (U.S. individual)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5721241		19980224
APPLICATION INFO.:	US 1995-466470		19950606 (8)

RELATED APPLN. INFO.:	Division of Ser. No. US 1993-146838, filed on 2 Nov 1993, now patented, Pat. No. US 5476855

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Shah, Mukund J.
ASSISTANT EXAMINER: Qazi, Sabiha N.
LEGAL REPRESENTATIVE: Nutter, McClennen & Fish, LLP
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
LINE COUNT: 1128
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel compounds are provided that are effective to inhibit the activity of DHUDase or UrdPase. Such compounds have the general formula ##STR1## where X is S or Se; Y H is I, F, Cl, Br, methoxy, benzyl, selenenylphenyl, or thiophenyl, and R.sub.1 is H or an acyclo tail having the general formula ##STR2## where R.sub.2 is H, CH.sub.2 OH or CH.sub.2 NH.sub.2 ; R.sub.3 is OH, NH.sub.2, or OCOCH.sub.2 CH.sub.2 CO.sub.2 H; and R.sub.4 is O, S, or CH.sub.2.

The compounds can be used in pharmaceutical compositions, along with various chemotherapeutic agents to increase the efficacy of the treatment. These compounds can also be used in methods of treating patients by coadministering or sequentially administering the enzyme inhibiting compounds with a chemotherapeutic agent effective to treat cancers, or viral, fungal, bacterial, or parasitic infections. The compounds have further utility in enhancing imaging. Further, they can be administered alone to prevent and/or treat disorders of pyrimidine catabolism and other physiological disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 55 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1998-557118 [47] WPIDS
DOC. NO. NON-CPI: N1998-434279
DOC. NO. CPI: C1998-166699
TITLE: Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): HANOVER, J A; LUBAS, W
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 80
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9844123	A2	19981008	(199847)*	EN	56
RW: AT BE CH DE DK ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9869425	A	19981022	(199910)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 9844123	A2	WO 1998-US6101	19980327
AU 9869425	A	AU 1998-69425	19980327

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9869425	A	Based on	WO 9844123

PRIORITY APPLN. INFO: US 1997-42270P 19970331
AN 1998-557118 [47] WPIDS
AB WO 9844123 A UPAB: 19981125
Isolated protein exhibiting **uridine** diphospho-N-acetylglucosamine:polypeptide beta -N-acetylglucosaminyl transferase (O-linked GlcNAc transferase) activity, OGT, is new. Also claimed are: (1) isolated DNA encoding OGT; (2) vectors comprising the DNA of (1) (optionally comprising regulatory nucleotide sequence operably linked to the DNA enabling protein expression in host cells, and (3) host cells containing vector, optionally also harbouring cellular components responsive to regulatory sequence.

USE - OGT is useful to assess predisposition toward type II diabetes in patients suspected of having hyperglycaemia that could evolve into this disease, by assaying OGT activity in red blood cells from a blood sample and comparing with activity in correlative samples from normal human subjects and patients with type II diabetes; patients are evaluated as predisposed if the activity falls within the range for the latter (claimed). Similarly, it can be used to assess predisposition toward **Alzheimer**'s disease, by comparing OGT activity in a sample from the central nervous system with that in correlative normal samples and samples from patients known to have **Alzheimer**'s disease (claimed). It can similarly be used to assess the metastatic potential of tumours, by assaying OGT activity in a tumour sample extract, comparing with correlative samples from normal subjects and those with metastatically active tumours, and diagnosing a tumour with metastatic potential if the activity falls within the range established for tumours with high metastatic activity (claimed). OGT can also be used to identify OGT inhibitors (claimed), especially in high-throughput assays (claimed), useful, e.g. in the treatment of diabetes mellitus, tumour-derived diseases and **Alzheimer**'s disease. Polynucleotides encoding OGT are useful to identify the genes and similar genes in other species.
Dwg.0/7

L5 ANSWER 4 OF 55 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED.
ACCESSION NUMBER: 1998-0416002 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Differential chromosome sensitivity to 5-azacytidine in Alzheimer's disease
AUTHOR: MARQUES PAYAO S. L.; DE ARRUDA CARDOSO SMITH M.; FERREIRA BERTOLUCCI P. H.
CORPORATE SOURCE: Departamento de Morfologia, Disciplina de Genetica, Paulista de Medicina, Sao Paulo, Brazil; Departamento de Neurologia Clinica, UNIFESP/Escola Paulista de Medicina, Sao Paulo, Brazil
SOURCE: Gerontology : (Basel), (1998), 44(5), 267-271, 31 refs.

ISSN: 0304-324X CODEN: GERNDJ
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Switzerland
LANGUAGE: English
AVAILABILITY: INIST-8223, 354000072684520030
AN 1998-0416002 PASCAL

AB Background: The methylation process in the DNA has been considered a control mechanism of gene activity, connected with genetic imprinting. 5-Aza-**cytidine** (5-AZC) is known to be a demethylation agent. Objective: We studied the cytogenetic effect of 5-AZC in **Alzheimer**'s disease patients and in two control groups. Methods: Peripheral lymphocyte cultures derived from 8 patients with **Alzheimer**'s disease and 8 elderly and 8 healthy young individuals, all female, were studied. The parameters investigated were: the undercondensation of constitutive heterochromatin of chromosomes 1, 9, and 16: the number of lesions in fragile sites 1q42 and 19q13; heterochromatin association, and the total number of induced lesions. Results: Our results showed a significantly increased frequency of undercondensation of chromosomes 1, 9, and 16 in **Alzheimer**'s disease patients when compared with elderly and young healthy groups. Conclusion: These results suggest that the demethylating action of 5-AZC could reveal differential gene activity in the **Alzheimer** group at the level of cellular division.

L5 ANSWER 5 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 1998:28527381 BIOTECHNO
TITLE: Run-on gene transcription in human neocortical nuclei: Inhibition by nanomolar aluminum and implications for neurodegenerative disease
AUTHOR: Lukiw W.J.; LeBlanc H.J.; Carver L.A.; McLachlan D.R.C.; Bazan N.G.
CORPORATE SOURCE: W.J. Lukiw, Louisiana State Univ. Medical Center, Neuroscience Center, Department of Ophthalmology, 2020 Gravier Street, New Orleans, LA 70112, United States.
SOURCE: Journal of Molecular Neuroscience, (1998), 11/1 (67-78), 81 reference(s)
CODEN: JMNEES ISSN: 0895-8696
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1998:28527381 BIOTECHNO
AB The incorporation of ¢α-.sup.3.sup.2P!- **uridine** triphosphate into DNA transcription products was examined in short post-mortem interval (PMI) human brain neocortical nuclei (n, 22; PMI, 0.5-24 h) using run-on gene transcription. Reverse Northern dot-blot hybridization of newly synthesized RNA against either total cDNA or Alu repetitive DNA indicated that human brain neocortical nuclei of up to 4-h PMI were efficient in incorporating radiolabel into new transcription products, after which there was a graded decline in de novo RNA biosynthetic capacity. To test the effects of 0-3000 nM concentrations of ambient aluminum on RNA polymerase I (RNAP I) and RNA polymerase II (RNAP II) transcription, dot blots containing 0.5, 1.0, 2.0, and 5.0 μg of DNA for (1) the human-specific Alu repetitive element (2) the neurofilament light (NFL) chain, and (3) glial fibrillary acidic protein

(GFAP) were Northern hybridized against newly synthesized radiolabeled total RNA. These DNAs represent heterogeneous nuclear RNA (hnRNA), neuronal-, and glial-specific markers, respectively. We report here a dose-dependent repression in the biosynthetic capabilities of brain RNAP II in the range of 50-100 nM aluminum, deficits similar to those previously described using a rabbit neocortical nuclei transcription system and at concentrations that have been reported in **Alzheimer** 's disease (AD) euchromatin. Transcription from RNAP II and the neuron-specific NFL gene in the presence of aluminum was found to be particularly affected. These findings support the hypothesis that brain gene transcription in the presence of trace amounts of ambient aluminum impairs mammalian brain DNA to adequately read out genetic information.

L5 ANSWER 6 OF 55 LIFESCI COPYRIGHT 2003 CSA
ACCESSION NUMBER: 2000:9430 LIFESCI
TITLE: RNA editing in plant mitochondria, cytoplasmic male sterility and plant breeding
AUTHOR: Araya, A.*; Zabaleta, E.; Blanc, V.; Begu, D.; Hernould, M.; Mouras, A.; Litvak, S.
CORPORATE SOURCE: Laboratoire REGER. EP 630. CNRS-Universite Victor Segalen Bordeaux 2. 1 rue Camille Saint Saeens. 33077 Bordeaux cedex. France
SOURCE: Electronic Journal of Biotechnology [Ejb], (19980415) vol. 1, no. 1, [np].
ISSN: 0717-3458.
DOCUMENT TYPE: Journal
TREATMENT CODE: General Review
FILE SEGMENT: W2
LANGUAGE: English
SUMMARY LANGUAGE: English
AB RNA editing in plant mitochondria is a post-transcriptional process involving the partial change of C residues into U. These C to U changes lead to the synthesis of proteins with an amino acid sequence different to that predicted from the gene. Proteins produced from edited mRNAs are more similar to those from organisms where this process is absent. This biochemical process involves **cytidine** deamination. The cytoplasmic male sterility (CMS) phenotype generated by the incompatibility between the nuclear and the mitochondrial genomes is an important agronomical trait which prevents inbreeding and favors hybrid production. The hypothesis that RNA editing leads to functional proteins has been proposed. This hypothesis was tested by constructing transgenic plants expressing a mitochondrial protein translated fom unedited mRNA. The transgenic "unedited" protein was addressed to the mitochondria leading to the appearance of **mitochondrial dysfunction** and generating the male sterile phenotype in transgenic tobacco plants. Male sterile plants were also obtained by expressing specifically a bacterial ribonuclease in the anthers. The economical benefits of artificially engineered male-sterile plants or carrying the (native) spontaneous CMS phenotype, implies the restoration to obtain fertile hybrids that will be used in agriculture. Restoration to fertility of transgenic plants was obtained either by crossing male-sterile plants carrying the "unedited" mRNA with plants carrying the same RNA, but in the antisense orientation or, in the case of plants expresing the ribonuclease, by crossing male-sterile plants with plants expressing an inhibitor specific of this enzyme.

L5 ANSWER 7 OF 55 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 1998078289 MEDLINE
DOCUMENT NUMBER: 98078289 PubMed ID: 9416333
TITLE: Blood-brain barrier disruption, HSP70 expression and apoptosis due to 3-nitropropionic acid, a mitochondrial toxin.
AUTHOR: Sato S; Gobbel G T; Li Y; Kondo T; Murakami K; Sato M; Hasegawa K; Copin J C; Honkaniemi J; Sharp F R; Chan P H
CORPORATE SOURCE: Department of Neurological Surgery, University of California, School of Medicine, San Francisco, USA.
CONTRACT NUMBER: AG 08938 (NIA)
NS 14543 (NINDS)
NS 25372 (NINDS)
+
SOURCE: ACTA NEUROCHIRURGICA. SUPPLEMENTUM, (1997) 70 237-9.
Journal code: 0140560. ISSN: 0065-1419.
PUB. COUNTRY: Austria
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980306
Last Updated on STN: 19980306
Entered Medline: 19980226

AB 3-Nitropropionic acid (3-NP), a mitochondrial toxin, induces apoptosis in the striatum. We wanted to determine if there was a relationship between **mitochondrial dysfunction**, disruption of the blood-brain barrier (BBB), and apoptosis. BBB disruption following intrastriatal injection of 3-NP was assessed by Evans blue leakage, brain water content, and by the expression of the 70 kDa heat shock protein (HSP70) and mRNA. Apoptosis was assessed by in situ terminal deoxynucleotidyl transferase-mediated **uridine** 5'-triphosphate-biotin nick end labeling (TUNEL) and gel electrophoresis to detect internucleosomal DNA fragmentation. Microscopic evidence of Evans blue leakage due to 3-NP was present only 3 hr after injection. Both internucleosomal DNA fragmentation and TUNEL-labeling did not appear until 24 hr after injection. HSP70 (protein and mRNA) was also elevated by 24 hr. There was a quantitative increase in Evans blue leakage and brain water content due to 3-NP by 3 days after injection. Our results suggest that BBB disruption is an early event followed by increased HSP70 expression and apoptosis. We speculate that 3-NP damages endothelial cells, leading to vasogenic edema and apoptosis.

L5 ANSWER 8 OF 55 USPATFULL
ACCESSION NUMBER: 96:97027 USPATFULL
TITLE: Methods for increasing uridine levels with L-nucleosides
INVENTOR(S): Sommadossi, Jean-Pierre, Birmingham, AL, United States
el Kouni, Mahmoud H., Birmingham, AL, United States
PATENT ASSIGNEE(S): The UAB Research Foundation, Birmingham, AL, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5567689		19961022	
APPLICATION INFO.:	US 1993-106225		19930813	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted

PRIMARY EXAMINER: Kunz, Gary L.
LEGAL REPRESENTATIVE: Geary, III, William C.Nutter, McClennen & Fish, LLP
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 752
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of increasing intracellular and plasma uridine levels comprising the coadministration or sequential administration of a compound from at least two of the following groups:

1) uridine phosphorylase inhibitors, uridine, cytidine, prodrugs of uridine, and prodrugs of cytidine;

2) a uridine secretion inhibiting compound such as dilazep or hexobendine; and

3) a compound which competes with uridine in renal transport mechanisms such as L-uridine, L-2',3'-dideoxyuridine, and D-2', 3'-dideoxyuridine.

The elevation of plasma and intracellular levels of uridine reduces the toxicity of pyrimidine nucleoside chemotherapeutic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 9 OF 55 USPATFULL
ACCESSION NUMBER: 95:112540 USPATFULL
TITLE: Enzyme inhibitors, their synthesis and methods for use
INVENTOR(S): el Kouni, Mahmoud, 4632 Round Forest Dr., Mt. Brook, AL, United States 35213-1832
Naguib, Fardos N. M., 4632 Round Forest Dr., Mt. Brook, AL, United States 35213-1832
Schinazi, Raymond F., 1524 Regency Walk Dr., Decatur, GA, United States 30033
PATENT ASSIGNEE(S): el Kouni, Mahmoud H., Mt. Brook, AL, United States (U.S. individual)
Naguib, Fardos N. M., Mt. Brook, AL, United States (U.S. individual)
Schinazi, F., Atlanta, GA, United States (U.S. individual)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5476855		19951219	
APPLICATION INFO.:	US 1993-146838		19931102	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Tsang, Cecilia
LEGAL REPRESENTATIVE: Geary, III, William C., Remillard, Jane E.Lahive & Cockfield
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
LINE COUNT: 994
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel compounds are provided that are effective to inhibit the activity of DHUDase or UrdPase. Such compounds have the general formula ##STR1## where X is S or Se; Y is I, F, Cl, Br, methoxy, benzyl, selenenylphenyl, or thiophenyl, and R.sub.1 is an acyclo tail having the general formula

##STR2## where R.sub.2 is H, CH.sub.2 OH or CH.sub.2 NH.sub.2 ; R.sub.3 is OH, NH.sub.2, or OCOCH.sub.2 CH.sub.2 CO.sub.2 H; and R.sub.4 is O, S, or CH.sub.2.

The compounds can be used in pharmaceutical compositions, along with various chemotherapeutic agents to increase the efficacy of the treatment. These compounds can also be used in methods of treating patients by coadministering or sequentially administering the enzyme inhibiting compounds with a chemotherapeutic agent effective to treat cancers, or viral, fungal, bacterial, or parasitic infections. The compounds have further utility in enhancing imaging. Further, they can be administered alone to prevent and/or treat disorders of pyrimidine catabolism and other physiological disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 10 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 1995:25050797 BIOTECHNO
TITLE: Respiratory-deficient human fibroblasts exhibiting defective mitochondrial DNA replication
AUTHOR: Bodnar A.G.; Cooper J.M.; Leonard J.V.; Schapira H.V.
CORPORATE SOURCE: Department of Clinical Neurosciences, Royal Free Hospital School Medicine, University of London,London NW3 2PF, United Kingdom.
SOURCE: Biochemical Journal, (1995), 305/3 (817-822)
CODEN: BIJOAK ISSN: 0264-6021
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1995:25050797 BIOTECHNO
AB We have characterized cultured skin fibroblasts from two siblings affected with a fatal **mitochondrial disease** caused by a nuclear genetic defect. Mitochondrial respiratory-chain function was severely decreased in these cells. Southern-blot analysis showed that the fibroblasts had reduced levels of mitochondrial DNA (mtDNA). The mtDNA was unstable and was eliminated from the cultured cells over many generations, generating the rho.sup.0 genotype. As the mtDNA level decreased, the cells became more dependent upon pyruvate and **uridine** for growth. Nuclear-encoded subunits of respiratory-chain complexes were synthesized and imported into the mitochondria of the mtDNA-depleted cells, albeit at reduced levels compared with the controls. Mitochondrial protein synthesis directed by the residual mtDNA indicated that the mtDNA was expressed and that the defect specifically involves the replication or maintenance of mtDNA. This is a unique example of a respiratory-deficient human cell line exhibiting defective mtDNA replication.

L5 ANSWER 11 OF 55 SCISEARCH COPYRIGHT 2003 ISI (R) DUPLICATE 4
ACCESSION NUMBER: 95:104003 SCISEARCH
THE GENUINE ARTICLE: QD409
TITLE: METABOLISM AND ACTIONS OF CDP-CHOLINE AS AN ENDOGENOUS COMPOUND AND ADMINISTERED EXOGENOUSLY AS CITICOLINE
AUTHOR: WEISS G B (Reprint)
CORPORATE SOURCE: M HURLEY & ASSOCIATES INC, 571 CENT AVE, MURRAY HILL, NJ, 07974 (Reprint)
COUNTRY OF AUTHOR: USA

SOURCE: LIFE SCIENCES, (20 JAN 1995) Vol. 56, No. 9, pp. 637-660.
ISSN: 0024-3205.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 184

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB CDP-choline, supplied exogenously as citicoline, has beneficial physiological actions on cellular function that have been extensively studied and characterized in numerous model systems. As the product of the rate-limiting step in the synthesis of phosphatidylcholine from choline, CDP-choline and its hydrolysis products (**cytidine** and choline) play important roles in generation of phospholipids involved in membrane formation and repair. They also contribute to such critical metabolic functions as formation of nucleic acids, proteins, and acetylcholine. Orally-administered citicoline is hydrolyzed in the intestine, absorbed rapidly as choline and **cytidine**, resynthesized in liver and other tissues, and subsequently mobilized in CDP-choline synthetic pathways. Citicoline is efficiently utilized in brain cells for membrane lipid synthesis where it not only increases phospholipid synthesis but also inhibits phospholipid degradation. Exogenously administered citicoline prevents, reduces, or reverses effects of ischemia and/or hypoxia in most animal and cellular models studied, and acts in head trauma models to decrease and limit nerve cell membrane damage, restore intracellular regulatory enzyme sensitivity and function, and limit edema. Thus, considerable accumulated evidence supports use of citicoline to enhance membrane maintenance, membrane repair, and neuronal function in conditions such as ischemic and traumatic injuries. Beneficial effects of exogenous citicoline also have been postulated and/or reported in experimental models for dyskinesia, Parkinson's disease, cardiovascular disease, aging, **Alzheimer**'s disease, learning and memory, and cholinergic stimulation.

L5 ANSWER 12 OF 55 ADISCTI COPYRIGHT 2003 (ADIS)
ACCESSION NUMBER: 1995:38451 ADISCTI
DOCUMENT NUMBER: 800378614
TITLE: Posatirelin for the treatment of late-onset Alzheimer's disease: a double- blind multicentre study vs citicoline and ascorbic acid.
ADIS TITLE: Posatirelin vs citicoline: therapeutic use. Alzheimer's disease.
AUTHOR: Parnetti L; Ambrosoli L; Abate G; Azzini C; Balestreri R; et al.
CORPORATE SOURCE: Perugia University, Perugia, Italy; Poli Industria Chimica S.p.A., Milan, Italy.
SOURCE: Acta Neurologica Scandinavica (Aug 1, 1995), Vol. 92, pp. 135-140
DOCUMENT TYPE: Study
REFERENCE: Alzheimer's Disease and Cognition Disorders
FILE SEGMENT: Summary
LANGUAGE: English
WORD COUNT: 718

L5 ANSWER 13 OF 55 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED. DUPLICATE
ACCESSION NUMBER: 1996-0052512 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1996 INIST-CNRS. All rights

TITLE (IN ENGLISH): CDP-choline : pharmacological and clinical review
AUTHOR: SECADES J. J.; FRONTERA G.
CORPORATE SOURCE: FISA medical dep., Barcelona, Spain
SOURCE: Methods and findings in experimental and clinical pharmacology, (1995), 17(SUPB), 1-54, 239 refs.
ISSN: 0379-0355
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Spain
LANGUAGE: English
AVAILABILITY: INIST-18217, 354000054975660010
AN 1996-0052512 PASCAL

AB **Cytidine** 5'-diphosphocholine, CDP-choline or citicoline, is an essential intermediate in the biosynthetic pathway of the structural phospholipids of cell membranes, especially in that of phosphatidylcholine. Upon oral or parenteral administration, CDP-choline releases its two principle components, **cytidine** and choline. When administered orally, it is absorbed almost completely, and its bioavailability is approximately the same as when administered intravenously. Once absorbed, the **cytidine** and choline disperse widely throughout the organism, cross the blood-brain barrier and reach the central nervous system (CNS), where they are incorporated into the phospholipid fraction of the membrane and microsomes. CDP-choline activates the biosynthesis of structural phospholipids in the neuronal membranes, increases cerebral metabolism and acts on the levels of various neurotransmitters. Thus, it has been experimentally proven that CDP-choline increases noradrenaline and dopamine levels in the CNS. Due to these pharmacological activities, CDP-choline has a neuroprotective effect in situations of hypoxia and ischemia, as well as improved learning and memory peformance in animal models of brain aging. Furthermore, it has been demonstrated that CDP-choline restores the activity of mitochondrial ATPase and of membranal Na.sup.+/K.sup.+ ATPase, inhibits the activation of phospholipase A.sub.2 and accelerates the reabsorption of cerebral edema in various experimental models. CDP-choline is a safe drug, as toxicological tests have shown ; it has no serious effects on the cholinergic system and it is perfectly tolerated. These pharmacological characteristics, combined with CDP-choline mechanisms of action, suggest that this drug may be suitable for the treatment of cerebral vascular disease, head trauma of varying severity and cognitive disorders of diverse etiology. In studies carried out on the treatment of patients with head trauma, CDP-choline accelerated the recovery from post-traumatic coma and the recuperation of walking ability, achieved a better final functional result and reduced the hospital stay of these patients, in addition to improving the cognitive and memory disturbances which are observed after a head trauma of lesser severity and which constitute the disorder known as postconcussion syndrome. In the treatment ofpatients with acute cerebral vascular disease of the ischemic type, CDP-choline accelerated the recovery of consciousness and motor deficit, attaining a better final result and facilitating the rehabilitation of these patients. The other important use for CDP-choline is in the treatment of senile cognitive impairment, which is secondary to degenerative diseases (e.g., **Alzheimer**'s disease) and to chronic cerebral vascular disease. In patients with chronic cerebral ischemia, CDP-choline improves scores on cognitive evaluation scales, while in patients with senile dementia of the

Alzheimer's type, it slows the disease's evolution. Beneficial neuroendocrine, neuroimmunomodulatory and neurophysiological effects have been described. CDP-choline has also been shown to be effective as co-therapy for Parkinson's disease. No serious side effects have been found in any of the groups of patients treated with CDP-choline, which demonstrates the safety of the treatment.

L5 ANSWER 14 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:466219 BIOSIS
DOCUMENT NUMBER: PREV199699188575
TITLE: Multi-infarct dementia: Modification of the P300 cognitive event-related potential in patients treated with the association of cytidine and uridine.
AUTHOR(S): Gallai, V.; Alberti, A.; Mazzotta, G.
CORPORATE SOURCE: Clin. Neurol., Univ. degli Studi, Perugia Italy
SOURCE: Rivista di Neuropsichiatria e Scienze Affini, (1995) Vol. 41, No. 1, pp. 1-9.
ISSN: 0035-6352.
DOCUMENT TYPE: Article
LANGUAGE: Italian
SUMMARY LANGUAGE: Italian; English
AB In Italy as in all western countries the mean age of the population is increasing progressively with consequent increase of the degenerative pathologies of the central nervous system, making extremely important the question of the cognitive decline. Although the majority of the dementia syndromes are due to **Alzheimer**'s disease and **Alzheimer** type, another important cause of dementia is Multi Infarct Dementia (MID), which is related to alterations of the cerebral blood flow. The present study was designed to evaluate the efficacy of **Cytidine** and **Uridine** in subjects with reduced mental capacity following to MID by means the event-related potential P300. The P300 is a neurophysiological method used to investigate cerebral electrical activity in the cognitive processing of information analysis. This potential was found to be altered in subjects affected by dementia. The present study was performed in 20 patients affected by multi-infarct dementia (MID) treated with **Cytidine** and **Uridine**. The patients, after a period of washout, were evaluated by electrophysiological examination performed at baseline and after 60 days. The event-related potential P300 was performed by an "odd-ball" paradigm with an acoustic modality; the patients were also assessed with the Digit Span, a sub-test of the Wechsler Adult Intelligence Scale to evaluate attention and short-term memory and with the Mini Mentale State. In the patients examined, the findings relevant to the study of the P300 showed a significant decrease in latency values compared to baseline. On the basis of this investigation it has been demonstrated that the variations in the registrations can be correlated to the improved neuronal activity following treatment with **Cytidine** and **Uridine**.

L5 ANSWER 15 OF 55 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 94:716280 SCISEARCH
THE GENUINE ARTICLE: PQ346
TITLE: AMYLOID PRECURSOR PROTEIN MESSENGER-RNA STABILITY IS CONTROLLED BY A 29-BASE ELEMENT IN THE 3'-UNTRANSLATED REGION
AUTHOR: ZAIDI S H E; MALTER J S (Reprint)
CORPORATE SOURCE: UNIV WISCONSIN HOSP & CLIN, DEPT PATHOL & LAB MED, A4-204-CSC, 600 HIGHLAND AVE, MADISON, WI, 53792

(Reprint); UNIV WISCONSIN, DEPT PATHOL & LAB MED, NEUROSCI PROGRAM, MADISON, WI, 53792; UNIV WISCONSIN, INST AGING, MADISON, WI, 53792
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (30 SEP 1994) Vol. 269, No. 39, pp. 24007-24013.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In the accompanying paper (Zaidi, S. H. E., Denman, R., and Malter, J. S. (1994) J. Biol. Chem. 269, 24000-24006) we demonstrate that in tumor and normal cells, multiple cytosolic proteins interact with a 29-base sequence in the 3'-untranslated region of amyloid precursor protein (APP) mRNA. These data suggested that APP gene expression may be modulated by regulated APP mRNA decay. We have investigated this prediction by measuring the decay rates of APP mRNA in resting and mitogen-treated peripheral blood mononuclear cells and H4 and K562 tumor cell lines. In resting peripheral blood mononuclear cells, APP mRNA decayed with a half-life of 4 h. Under these conditions, the activity of APP mRNA-binding proteins was not detectable. After activation, binding protein activities were induced, and APP mRNA decay was blocked with a half-life of >12 h. In log phase neuronal or lymphoid tumor cell lines, binding activity was constitutively present and APP mRNA displayed a half-life of >12 h. Protein synthesis inhibition by cycloheximide had no effect on APP mRNA decay in normal or tumor cells. Transfected wild type or mutant APP mRNAs that lacked the 29-base region were stable (t(1/2) > 10 h) in K562 tumor cells. Therefore, we conclude that the 29-base region functions in cis to destabilize APP mRNA in resting, normal cells. Upon activation APP mRNA-binding proteins are induced, interact with the 29-base region, and likely participate in stabilization of the mRNA.

L5 ANSWER 16 OF 55 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 94:716279 SCISEARCH
THE GENUINE ARTICLE: PQ346
TITLE: MULTIPLE PROTEINS INTERACT AT A UNIQUE CIS-ELEMENT IN THE 3'-UNTRANSLATED REGION OF AMYLOID PRECURSOR PROTEIN MESSENGER-RNA
AUTHOR: ZAIDI S H E; DENMAN R; MALTER J S (Reprint)
CORPORATE SOURCE: UNIV WISCONSIN HOSP & CLIN, DEPT PATHOL & LAB MED, A4-204-CSC, 600 HIGHLAND AVE, MADISON, WI, 53792 (Reprint); UNIV WISCONSIN, DEPT PATHOL & LAB MED, NEUROSCI PROGRAM, MADISON, WI, 53792; UNIV WISCONSIN, INST AGING, MADISON, WI, 53792; NEW YORK STATE INST BASIC RES DEV DISABIL, STATEN ISL, NY, 10314
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (30 SEP 1994) Vol. 269, No. 39, pp. 24000-24006.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Growing evidence suggests that Alzheimer's disease results from

dysregulated production and deposition of beta-amyloid in the central nervous system. beta-Amyloid is derived from proteolytic processing of one of multiple amyloid precursor protein (APP) isoforms. The production of APP in many somatic tissues and tumor cell lines provides a more accessible model to study the regulation of APP gene expression. Recent data suggest that APP mRNAs accumulate in activated lymphocytes and neuronal tumor lines. We are interested in defining the contribution of alterations in stability to changes in steady-state APP mRNA levels in these model systems. Herein we demonstrate by mobility shift assay that the 3'-untranslated region of APP RNAs which contain a contiguous 29-base region interacts in vitro with multiple mRNA-binding proteins found in cytosolic lysates prepared from normal and transformed human cells. UV cross-linking of radiolabeled APP RNAs to cytosolic protein extracts followed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis identified six distinct RNA-protein complexes of 42, 47, 65, 73, 84, and 104 kDa Competition assays with APP, AU-rich, or irrelevant RNAs demonstrated that binding was specific and in some cases preferential for AU- or U-rich sequences by which we tentatively place the binding site of the proteins along the 29-base region. APP mRNA-binding proteins were constitutively active in all tumor lines examined as web as at diminished levels in whole human brain cytosolic lysates. The core element is AU-rich and highly conserved between human and some murine APP mRNAs. In the accompanying paper (Zaidi, S. H. E. and Malter, J. S. (1994) J. Biol. Chem. 269, 24007-24013) we show that this 29-base element in the 3'-untranslated region regulates the stability of APP mRNA. Cumulatively these data suggest that steady-state APP mRNA levels are modulated by cytosolic protein-RNA interactions.

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DUPLICATE

ACCESSION NUMBER:	1995-0163958 PASCAL
COPYRIGHT NOTICE:	Copyright .COPYRGT. 1995 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH):	Brain mapping activity and mental performance after chronic treatment with CDP-choline in Alzheimer's disease
AUTHOR:	FRANCO-MASIDE A.; CAAMANO J.; GOMEZ M. J.; CACABELOS R.
CORPORATE SOURCE:	Inst. cent. nervous system disorders, basic clin. neuros. res. cent., dep. digital diagnosis clin. neurosci., 15080 La Coruna, Spain
SOURCE:	Methods and findings in experimental and clinical pharmacology, (1994), 16(8), 597-607, 45 refs. ISSN: 0379-0355
DOCUMENT TYPE:	Journal
BIBLIOGRAPHIC LEVEL:	Analytic
COUNTRY:	Spain
LANGUAGE:	English
AVAILABILITY:	INIST-18217, 354000057830070070

AN 1995-0163958 PASCAL
CP Copyright .COPYRGT. 1995 INIST-CNRS. All rights reserved.
AB CDP-choline participates in brain phospholipid metabolism and acts as an endogenous intermediate in a biosynthetic pathway incorporating free choline into phosphatidylcholine and choline plasmalogens in several tissues, including the central nervous system (CNS). In patients with chronic cerebrovascular disorders, CDP-choline reduces the slow delta frequencies and increases alpha activity in spectral electroencephalogram

analysis. We have studied the effect of CDP-choline (**cytidine** -5-diphosphate-choline; 1000 mg/day x 30 days, p.o.) on brain electrical activity mapping and mental performance in 19 **Alzheimer**'s disease (AD) patients (10 males/9 females; age:66.21±1.48 years; Mini-Mental State Examination (MMSE): 26.55±1.22, Spanish version maximum score 35)

L5 ANSWER 18 OF 55 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED. DUPLICATE

ACCESSION NUMBER: 1994-0437018 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1994 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): CDP-choline-induced blood histamine changes in Alzheimer's disease
AUTHOR: FERNANDEZ-NOVOA L.; ALVAREZ X. A.; FRANCO-MASIDE A.; CAAMANO J.; CACABELOS R.
CORPORATE SOURCE: Complutense univ. medical school, dep. human physiology, neurogerontology unit, 28040 Madrid, Spain
SOURCE: Methods and findings in experimental and clinical pharmacology, (1994), 16(4), 279-284, 38 refs. ISSN: 0379-0355
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Spain
LANGUAGE: English
AVAILABILITY: INIST-18217, 354000045285930070
AN 1994-0437018 PASCAL
CP Copyright .COPYRGT. 1994 INIST-CNRS. All rights reserved.
AB Histamine (HA) is a known neurotransmitter with a wide spectrum of biological actions at the central and peripheral levels. Recently, it has been found that HA is involved in the regulation of immune cell function, acting as an immunomodulator A hyperactivation in the histaminergic system has been demonstrated in **Alzheimer**'s disease (AD), including increased levels of HA in brain, serum, a cerebrospinal fluid of AD patients. In addition, changes in phospholipid metabolism and neuroimmune function have been reported in AD. CDP-choline (**cytidine**-5-diphosphate-choline) participates in the phospholipid metabolism pathway incorparating free choline into phosphatidyl-choline and choline plasmalogens in several tissues, including the central nervous system

L5 ANSWER 19 OF 55 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 8

ACCESSION NUMBER: 1994:548887 CAPLUS
DOCUMENT NUMBER: 121:148887
TITLE: Effects of CDP-choline on cognition and cerebral hemodynamics in patients with Alzheimer's disease
AUTHOR(S): Caamano, J.; Gomez, M.J.; Franco, A.; Cacabelos, R.
CORPORATE SOURCE: Basic Clin. Neurosci. Res. Cent., Inst. C.N.S. Dis., La Coruna, Spain
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (1994), 16(3), 211-18 CODEN: MFEPDX; ISSN: 0379-0355
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CDP-choline (**cytidine**-5-diphosphate-choline) is an acetylcholine precursor frequently used in cerebrovascular disorders and psychoorg. syndromes. Furthermore, several authors have demonstrated the pos.

effects of CDP-choline on cognitive disorders and memory deficits. In the present study, the effects of CDP-choline (1000 mg/day, p.o. for 1 mo) on cognition, evaluated by the Mini-Mental State Examination (MMSE) of Folstein et al., and on blood flow velocities, measured by transcranial Doppler ultrasonog. (TCD), were investigated in patients with **Alzheimer** 's disease: (AD, n = 20, age: 66.75 +/-6.73 yr, range: 57-78 yr). Cognitive function was measured by means of the MMSE in basal conditions (A) and after 1 mo of treatment with CDP-choline (C). TCD measures were taken through the temporal window for right (MCA-R) and left (MCA-L) middle cerebral arteries with a 2 MHz pulsed transducer using a TC-2000S in basal conditions (A), 1 h after the administration of CDP-choline (B) and after 1 mo of treatment with CDP-choline (C). MMSE scores were significantly increased ($p < 0.005$) in patients with early-onset Alzheimer's disease (EOAD) after CDP-choline treatment. Moreover, the orientation subtest significantly increased in the global group of AD patients ($p < 0.01$) and in EOAD patients ($p < 0.02$). Significant differences ($p < 0.05$) were also found in MCA-L and MCA-R measures between recordings. These results suggest that CDP-choline influences cognitive and cerebrovascular function in Alzheimer's disease, probably through a mechanism linked to an immunogenic and/or neurotrophic effect at the microvascular niche. However, a direct vasoactive effect on the vascular endothelium cannot be ruled out.

L5 ANSWER 20 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 1994:24023911 BIOTECHNO
TITLE: Enzymatic amplification of synthetic oligodeoxyribonucleotides: Implications for triplet repeat expansions in the human genome
AUTHOR: Behn-Krappa A.; Doerfler W.
CORPORATE SOURCE: Institute of Genetics, University of Cologne,D-50931 Cologne, Germany.
SOURCE: Human Mutation, (1994), 3/1 (19-24)
CODEN: HUMUE3 ISSN: 1059-7794
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1994:24023911 BIOTECHNO
AB The triplet repeat sequences (CGG)(n), (GCT)(n), and (CAG)(n), which naturally occur in the human genome, can be autonomously expanded in human DNA by an as yet unknown mechanism. These in part excessive expansions have been causally related to human genetic diseases, the fragile X (Martin-Bell) syndrome, to myotonic dystrophy (Curschmann-Steinert), to spinal and bulbar muscular atrophy (Kennedy disease), and recently to **Huntington** disease. A GCC trinucleotide repeat was found to be expanded and methylated in the fragile site FRAXE on the human X chromosome. These findings were associated with mental retardation (Knight et al., 1993). In spinocerebellar ataxia type 1 (SCA1), a polymorphic CAG repeat was found to be unstable and expanded in individuals with that disease (Orr et al., 1993). We have demonstrated in in vitro experiments that the synthetic oligodeoxyribonucleotides (CGG).sub.1.sub.7, (CGG).sub.1.sub.2, (GCC).sub.1.sub.7, (CG).sub.2.sub.5, (CTG).sub.1.sub.7, or (CAG).sub.1.sub.7 plus (GTC).sub.1.sub.7, in the absence of added natural DNA, can be expanded with Taq polymerase in the polymerase chain reaction (PCR). Some expansion can already be detected after 4 PCR cycles. The E. coli Klenow DNA polymerase also functions in a similar amplification and

expansion reaction performed at 37°C without cycling. Other oligodeoxyribonucleotides, like, (CGG).sub.7, (CGGT).sub.1.sub.3, or (TAA).sub.1.sub.7, are devoid of this property or have very low activity. The **cytidine**-methylated polymers (GCC).sub.1.sub.7 or (CG).sub.2.sub.5 yield expansion products of considerably reduced chain lengths. The expansion of the polymer (CGG).sub.1.sub.7 is affected by **cytidine** methylation to a lesser degree. A specific sequence and/or secondary structure and high CG content appear to be requirements for this expansion reaction by a possible slippage mechanism. Does this in vitro reaction mimic elements of the amplification events in the human genome?

L5 ANSWER 21 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 1993:23304139 BIOTECHNO
TITLE: Nuclear complementation restores mtDNA levels in cultured cells from a patient with mtDNA depletion
AUTHOR: Bodnar A.G.; Cooper J.M.; Holt I.J.; Leonard J.V.; Schapira A.H.V.
CORPORATE SOURCE: Department of Neurological Science, Royal Free Hospital Sch. of Medicine, Rowland Hill Street,London NW3 2PF, United Kingdom.
SOURCE: American Journal of Human Genetics, (1993), 53/3 (663-669)
CODEN: AJHGAG ISSN: 0002-9297
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1993:23304139 BIOTECHNO
AB We have studied cultured skin fibroblasts from a patient with a fatal **mitochondrial disease** manifesting soon after birth. These fibroblasts were found to grow only in the presence of pyruvate and **uridine**, a characteristic of cells lacking mtDNA (rho.sup.0 cells). Southern blot and PCR analyses confirmed that the patient's fibroblasts contained less than 2% of control levels of mtDNA. Biochemical analyses indicated that the activities of all the respiratory-chain enzymes were severely decreased in mitochondria isolated from these fibroblasts. In order to elucidate the underlying molecular defect, cell fusions were performed between enucleated fibroblasts from this patient and a human-derived rho.sup.0 cell line (rho.sup.0A549.B2). The resulting cybrids were plated in medium lacking pyruvate and **uridine**, to select for the restoration of respiratory-chain function. Complementation was observed between the nuclear genome of the rho.sup.0A549.B2 cells and the mtDNA of the patient's cells, restoring mtDNA levels and respiratory-chain function in the cybrid cells. These results indicate that mtDNA depletion in our patient is under the control of the nuclear genome.

L5 ANSWER 22 OF 55 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:166580 CAPLUS
DOCUMENT NUMBER: 118:166580
TITLE: RNA metabolism in human brain during aging and in Alzheimer's disease. RNA synthesis in the nuclei isolated from postmortem brain tissue
AUTHOR(S): Sajdel-Sulkowska, Elizabeth M.
CORPORATE SOURCE: Neurobiol. Lab., Massachusetts Gen. Hosp., Boston, MA, USA

SOURCE: Advances in Behavioral Biology (1992), 40(Treat. Dementias), 397-406
CODEN: ADBBBW; ISSN: 0099-6246
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present studies provide exptl. evidence for the preservation of transcriptional processes in the postmortem human brain. Cortical tissue specimens from a total of 29 control and **Alzheimer**'s Disease cases, 56-91 yr of age, with postmortem intervals of 1.0-3.0 h were examined When incubated under organotypic tissue culture conditions, autopsied tissues incorporated [3H]**uridine** into alkaline hydrolyzed material for at least 90 min. Incorporation of labeled nucleotide into hydrolyzate or in phenol exts. was sensitive to Actinomycin D, α-amanitin and DRB. The specific activity of RNA ranged from 2.1-8.8 + 105 dpm/mg RNA. Nuclei prepared from the postmortem tissue incorporates 32P UTP to the specific activity of 1.3 + 109 dpm/mg RNA. The high specific activity of RNA synthesized by nuclei allowed us to characterize newly made RNA. Two lines of expts.: RNase protection assay and RNAPCR suggest that the RNA synthesized by the nuclei prepared from the human postmortem tissue reflects the RNA normally made in vivo.

L5 ANSWER 23 OF 55 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 1992-46037 DRUGU P
TITLE: Medicinal Benefits of the Mushroom Ganoderma.
AUTHOR: Jong S C; Birmingham J M
LOCATION: Rockville, Maryland, United States
SOURCE: Adv.Appl.Microbiol. (37, 101-34, 1992) 11 Fig. 1 Tab. 142 Ref.
CODEN: ADAMAP ISSN: 0065-2164
AVAIL. OF DOC.: Mycology and Botany Department, American Type Culture Collection, Rockville, Maryland 20852, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 1992-46037 DRUGU P
AB Medicinal properties and patented products of extracts of the mushroom Ganoderma are reviewed. Chemicals isolated from various species include ergosterol, fungal lysozyme, acid protease, proteins and saccharides, adenine, adenosine, uracil, **uridine** and D-mannitol, as well as bitter triterpenes (ganoderic, lucidenic, ganodermic and ganoderenic acids, lucidone, ganoderal and ganoderols). Medicinal properties include antitumor, immunomodulatory, cardiovascular, respiratory and CNS effects, effects on protein synthesis, liver protection and detoxification, muscular dystrophy and radiation damage and extracts are included in antitumor, hypotensive, hypoglycemic, hypocholesterolemic, skin and bath, hair tonics, liver function stimulants, drinks and **Alzheimer**'s disease treatments.
ABEX The Chinese mushroom Ganoderma is being produced on a large scale. G. lucidum yields about 100 different triterpenoids, mostly ganoderic (A, B, C, J and T-Z) and lucidenic acids, that vary with strain and location in the plant (fruiting body vs. mycelium). Lucidones, ganoderenic acids, epoxyganoderols, sterols, ganoderiols and ganolucidic acids (varying bitterness), have been isolated. High molecular weight polysaccharides from cell walls of G. applanatum and G. lucidum have antitumor activity in mice. A homolanosteroid carboxyacetylquercinic acid from wild Javan Ganoderma inhibits EBV activation but high levels are toxic.

Polysaccharide D6 from G. lucidum fruiting body increases serum, liver and bone marrow protein synthesis in mice, G. lucidum and G. capense spores have CNS activity, while mycelial extracts increase resistance to digitoxin or indometacin toxicity (ganoderic acids R and S are also antihepatotoxic in rats). Cardiotonic, hypotensive, hypocholesterolemic, hypoglycemic, antitussive (ganoderan B), expectorant, antiaggregant, antiinflammatory, immunomodulatory (polysaccharide BN3C, Ling-Zhi-8 protein) and antimyotonia (G. japonicum) effects occur. Antitumor (beta-glucan ganoderan, hybrid cells), liver, hypotensive (G. lucidum powder/extract), hypocholesterolemic (fermentation product), hypoglycemic, immunomodulatory (anti-retrovirus, immunosuppressant, phagocyte activator), antibiotic-bacteriolytic enzyme, antimutagenic, antibronchitis and **Alzheimer**'s disease treatments and beverages (laxatives) with isolates or extracts are patented. (E8/LJ)

L5 ANSWER 24 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:491437 BIOSIS
DOCUMENT NUMBER: BR43:100637
TITLE: THE EXPRESSION OF THE AMYLOID PRECURSOR PROTEIN APP IS REGULATED BY TWO GC-ELEMENTS IN THE PROMOTER.
AUTHOR(S): POLLWEIN P; POLLWEIN R; MASTERS C L; BEYREUTHER K
CORPORATE SOURCE: CENT. MOL. BIOL. HEIDELBERG, UNIV. HEIDELBERG, D-6900 HEIDELBERG, GER.
SOURCE: THIRD INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED DISORDERS, ABANO TERME, ITALY, JULY 12-17, 1992. NEUROBIOL AGING, (1992) 13 (SUPPL 1), S71-S72. CODEN: NEAGDO. ISSN: 0197-4580.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L5 ANSWER 25 OF 55 SCISEARCH COPYRIGHT 2003 ISI (R) DUPLICATE 11
ACCESSION NUMBER: 91:204210 SCISEARCH
THE GENUINE ARTICLE: FE557
TITLE: AN RNA CODING FOR THE **ALZHEIMER** AMYLOID PRECURSOR PROTEIN INTERACTS INVITRO WITH THE ADENOSINE-**URIDINE** BINDING-FACTOR
AUTHOR: MALTER J (Reprint); MILLER D L; DENMAN R
CORPORATE SOURCE: TULANE UNIV, SCH MED, DEPT PATHOL, NEW ORLEANS, LA, 70112; NEW YORK STATE INST BASIC RES DEV DISABILITIES, STATEN ISL, NY, 10314
COUNTRY OF AUTHOR: USA
SOURCE: FASEB JOURNAL, (1991) Vol. 5, No. 6, pp. A1606.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L5 ANSWER 26 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1990:120063 BIOSIS
DOCUMENT NUMBER: BR38:54273
TITLE: CHOLINE METABOLISM IN CHOLINERGIC NEURONS IMPLICATIONS FOR THE PATHOGENESIS OF NEURODEGENERATIVE DISEASES.
AUTHOR(S): WURTMAN R J; KRZYSZTOF BLUSZTAJN J; ULUS I H; G-COVIELLA I L; BUYUKUYSAL R L; GROWDON J H; SLACK B E
CORPORATE SOURCE: DEP. BRAIN COGNITIVE SCI., MASS. INST. TECHNOL., CAMBRIDGE, MASS. 02139.

SOURCE: WURTMAN, R. J., ET AL. (ED.). ADVANCES IN NEUROLOGY, VOL. 51. ALZHEIMER'S DISEASE. XXVII+282P. RAVEN PRESS: NEW YORK, NEW YORK, USA. ILLUS, (1990) 0 (0), 117-126.
CODEN: ADNRA3. ISSN: 0091-3952. ISBN: 0-88167-574-1.
FILE SEGMENT: BR; OLD
LANGUAGE: English

L5 ANSWER 27 OF 55 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 12
ACCESSION NUMBER: 1989:470975 CAPLUS
DOCUMENT NUMBER: 111:70975
TITLE: Phosphoethanolamine for treatment of Alzheimer's disease
INVENTOR(S): Appel, Stanley H.
PATENT ASSIGNEE(S): Baylor College of Medicine, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8809171	A1	19881201	WO 1988-US1693	19880518
W: AU, DK, JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8817909	A1	19881221	AU 1988-17909	19880518

PRIORITY APPLN. INFO.: US 1987-51897 19870519
US 1988-188005 19880511
WO 1988-US1693 19880518

OTHER SOURCE(S): MARPAT 111:70975
AB Stereoisomers of the ethanolamines R1NHCHR2CHR3R4 (R1 = H, alkyl; R2, R3 = H, alkyl, CO2M; R4 = OH, PO3H2, OPO3H2, **cytidine**-5'-diphosphate or their salts; M = H, cation) are drugs for the treatment of **Alzheimer**'s disease. Phosphoethanolamine, extracted from the calf brain, stimulated acetylcholine biosynthesis, in vitro, with a ED50 value of 5 μM. This finding is important due to the deficiency of acetylcholine in **Alzheimer**'s disease.

L5 ANSWER 28 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. DUPLICATE 13
ACCESSION NUMBER: 1988:355300 BIOSIS
DOCUMENT NUMBER: BA86:50778
TITLE: PHOSPHORUS-31 NMR STUDY OF THE BRAIN IN ALZHEIMER'S DISEASE.
AUTHOR(S): PETTEGREW J W; MOOSSY J; WITHERS G; MCKEAG D; PANCHALINGAM K
CORPORATE SOURCE: LAB. NEUROPHYSICS, DEP. PSYCHIATRY AND NEUROL., UNIV. PITTSBURGH, WESTERN PSYCHIATRIC INST. AND CLINIC, 3811 O'HARA ST., PITTSBURGH, PA. 15213.
SOURCE: J NEUROPATHOL EXP NEUROL, (1988) 47 (3), 235-248.
CODEN: JNENAD. ISSN: 0022-3069.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The histopathological hallmarks of **Alzheimer**'s disease have long been considered to be neurofibrillary tangles (NFT) and neuritic (senile) plaques (SP). Neither of these structures, however, are unique to

Alzheimer's disease, and both probably represent end-stage markers of the disorder. NFT have been demonstrated in many disorders; SP occur in small numbers with normal aging. Evidence is presented for elevation of phosphomonoesters (PME) in **Alzheimer**'s brain compared to non-**Alzheimer**'s diseased controls and normal controls. The PME detected by 31P nuclear magnetic resonance (NMR) spectroscopy of autopsy brain are predominantly anabolic precursors of membrane phospholipids. Elevated PME could be secondary to a metabolic block at the rate-limiting enzyme in membrane phospholipid synthesis, which is **cytidine** triphosphate (CTP):phosphocholine (or phosphoethanolamine)cytidyltransferase (EC 2.7.7.15). Elevated PME could also be secondary to decreased breakdown of PME by phospholipase D activity. Since CTP:phosphocholine cytidyltransferase is inactivated by phosphorylation and since there is independent evidence for hyperphosphorylation of tau and MAP-2 proteins in AD brain, enhanced protein kinase activity could be a common factor. Preliminary evidence suggests that PME could interact with N-methyl-D-aspartate receptors and potentially act as false neurotransmitters. Further studies will be needed to investigate these possibilities.

L5 ANSWER 29 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1988:170565 BIOSIS
DOCUMENT NUMBER: BR34:85177
TITLE: RADIOACTIVE **URIDINE** INCORPORATION INTO RNA BY POSTMORTEM HUMAN BRAIN TISSUE EVIDENCE FOR POSTMORTEM TRANSCRIPTION IN THE **ALZHEIMER** BRAIN.
AUTHOR(S): SAJDEL-SULKOWSKA E M; MAROTTA C A
CORPORATE SOURCE: DEP. PSYCHIATRY, HARVARD MED. SCH., BELMONT, MA 02178, USA.
SOURCE: 17TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, NEW ORLEANS, LOUISIANA, USA, NOVEMBER 16-21, 1987. SOC NEUROSCI ABSTR, (1987) 13 (2), 1326.
CODEN: ASNEE5.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L5 ANSWER 30 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 1986:16049347 BIOTECHNO
TITLE: Intravenous uridine treatment antagonizes hypoglycaemia-induced reduction in brain somatostatin-like immunoreactivity
AUTHOR: Agnati L.F.; Fuxe K.; Eneroth P.; et al.
CORPORATE SOURCE: Department of Human Physiology, University of Modena, Modena, Italy.
SOURCE: Acta Physiologica Scandinavica, (1986), 126/4 (525-531)
CODEN: APSCAX
DOCUMENT TYPE: Journal; Article
COUNTRY: Sweden
LANGUAGE: English
AN 1986:16049347 BIOTECHNO
AB By means of radioimmunoassay procedures, cholecystokinin-(CCK) and somatostatin-(SRIF) like immunoreactivity have been studied in the dorsal hippocampal formation and in the frontoparietal cortex of the male rat in insulin-induced hypoglycaemia, leading to an isoelectric EEG pattern. It has been demonstrated that severe hypoglycaemia of 40-min-duration produces a disappearance of SRIF but not of CCK-like immunoreactivity in

both cortical regions. It was found that an i.v. injection of **uridine** but not of saline could significantly counteract the disappearance of SRIF-like immunoreactivity induced by severe hypoglycaemia in both cortical areas. **Uridine** did not by itself change plasma glucose levels. It is suggested that **uridine** may prevent release and/or increase synthesis of cortical SRIF peptides in severe hypoglycaemia, possibly due to an action on the metabolism (e.g. by enhancing the resynthesis of phosphatidyl inositol) within the tissue of the cerebral cortex and/or on putative pyrimidine binding sites in the brain controlling SRIF synthesis and/or release. It is possible that **uridine** in this way may improve recovery of neuronal function within SRIF-immunoreactive neurons of the cerebral cortex severe hypoglycaemia (which also may be true in other states of reduced metabolic support). These findings suggest a possibility to use **uridine** in the treatment of **Alzheimer**'s disease and Status epilepticus.

L5 ANSWER 31 OF 55 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1984-290125 [47] WPIDS
DOC. NO. CPI: C1984-123174
TITLE: Compsn. containing amino acid and choline or precursor - useful for treating neurological disease or ageing.
DERWENT CLASS: B05
INVENTOR(S): WURTMAN, R J
PATENT ASSIGNEE(S): (MASI) MASSACHUSETTS INST TECHNOLOGY
COUNTRY COUNT: 16
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 125900	A	19841121	(198447)*	EN	20
R: AT BE CH DE FR GB IT LI LU NL SE					
JP 60214734	A	19851028	(198549)		
ES 8602409	A	19860316	(198620)		
US 4624852	A	19861125	(198650)		
CA 1228301	A	19871020	(198746)		
IL 71819	A	19871231	(198809)		
US 4737489	A	19880412	(198817)		
US 4775665	A	19881004	(198842)		
EP 125900	B	19890823	(198934)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE					
JP 01041124	B	19890904	(198939)		
DE 3479477	G	19890928	(198940)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 125900	A	EP 1984-303195	19840511
JP 60214734	A	JP 1984-94739	19840514
ES 8602409	A	ES 1984-532873	19840515
US 4624852	A	US 1984-613000	19840521
US 4737489	A	US 1984-685591	19841221
US 4775665	A	US 1987-102062	19870924

PRIORITY APPLN. INFO: US 1983-495202 19830516; US 1984-613000

19840521; US 1984-685591 19841221; US 1987-102062 19870924

AN 1984-290125 [47] WPIDS

AB EP 125900 A UPAB: 19930925

Pharmaceutical compsn. comprises (a) at least 1 of phenylalanine, tyrosine, threonine or tryptophan; and (b) choline and/or its precursor.

USE/ADVANTAGE - The compsn. potentiates the effect of neurotransmitter precursors in the brain and so is useful in relieving the adverse effects of neurological disease or ageing in a patient. Dose is sufficient for (b) to raise the blood stream choline to 10-50 ng/ml.so that effective amounts of acetylcholine are produced.

0/0

ABEQ EP 125900 B UPAB: 19930925

A pharmaceutical composition comprising (a) at least one amino acid selected from phenylalanine, tyrosine, threonine, and tryptophan; and (b) choline, a choline precursor or a mixture of choline and its precursor in amounts sufficient to cause a synergistic enhancement of neurotransmission; the composition being substantially free of other amino acids.

ABEQ US 4624852 A UPAB: 19930925

New process to releive neurological disease or aging comprises admin. of tryptophane (or other amino acid) and choline or choline precursor to raise blood choline level to 10-50 n moles/ml and release brain acetylcholine. Choline may be choline salt or ester, sphingomyelin, lethicin, **cytidine**, diphosphochloine or acylglycerylcholine of formula (I) in which FA1 and FA2 are 6-26C fatty acid residues.

USE - In treatment of neurological disease e.g. senility and **Alzheimer**'s and Parkinson's diseases by acting synergistically to increase release of both chlinergic and dopaminergic neurotransmitters. Dosage e.g. 1-30(3-20)g/day choline and 10-200 mg/kg tryptophan.

ABEQ US 4737489 A UPAB: 19930925

New treatment for neurological disease or ageing comprises co-admin. amino acid viz. Pla, Tyr, Thr, to increase release of brain neurotransmitter for which it is precursor and 10-50 n moles/ml of choline or choline precursor viz. choline ester, sphingmyelon, **cytidine**-di-phospho-choline or an acyl glycerophosphocholine of formula (I) or lethicin to release brain acetylcholine. In (I) FA1 and FA2 are 6-26C fatty acid residues.

USE/ADVANTAGE - By increasing blood acetylcholine, dopamine, norepinephrine, ephridine, etc. cholinergic, catecholaminergic and serotoninergic and glycinergic neutrons are synergistically stimulated resulting in rapid forming of synapses from remaining cells after loss e.g. in **Alzheimer**'s, Parkinson's diseases, and senility.

ABEQ US 4775665 A UPAB: 19930925

Relieving adverse effects of neurological disease ageing comprises administering an amino acid viz. Pla, Tyr, Thr, Trp or mixt. to release cns neutrotransmitter and cpd. to raise blood choline to 10-50 nM/ml release brain AcCh, viz. choline opt. as salt or ester sphingomyelin, cytidine-dihospho-choline or acyglycerophosphocholine of formula (I), where FA1 and FA2 are each 6-26C fatty acid residues and insulin-releasing carbohydrate. Compsn. described is also claimed.

ADVANTAGE - Components act synergistically to potentiate cns neurotransmitters of which the amino acids are pre choline and 0.5-250 mg/kg amino acid.

L5 ANSWER 32 OF 55 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1984-244938 [40] WPIDS

DOC. NO. CPI: C1984-103379

TITLE: Treating disturbances of central and peripheral nervous systems - with cytidine mono phosphate of galactono-nulosaminic acid derivative.
DERWENT CLASS: B03
INVENTOR(S): DECORTE, E; MICCOLI, P
PATENT ASSIGNEE(S): (CRCH) CRC CIA DI RICERCHE CHIM SA
COUNTRY COUNT: 14
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 120328	A	19841003	(198440)*	EN	26
R: AT BE CH DE FR GB LI LU NL SE					
JP 60006618	A	19850114	(198508)		
CA 1219539	A	19870324	(198716)		
US 4704361	A	19871103	(198746)		
EP 120328	B	19881019	(198842)#	EN	
R: AT BE CH DE FR GB LI LU NL SE					
CA 1243971	A	19881101	(198848)		
DE 3474632	G	19881124	(198848)		
JP 02016732	B	19900418	(199019)		
IT 1175061	B	19870701	(199029)#		
IT 1175084	B	19870701	(199029)		
US 5070079	A	19911203	(199151)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 120328	A	EP 1984-102059	19840228
JP 60006618	A	JP 1984-36341	19840229
US 4704361	A	US 1984-584805	19840229
JP 02016732	B	JP 1984-36341	19840229
US 5070079	A	US 1990-560239	19900723

PRIORITY APPLN. INFO: IT 1983-83371 19830420; IT 1983-34183 19830301; IT 1983-83341 19830301
AN 1984-244938 [40] WPIDS
AB EP 120328 A UPAB: 19970828
Compsn. for treatment of states related to disturbances of the nervous stimulus in the CNS and PNS comprises **cytidine** monophosphate of 5-acetamido-3,5-dideoxy-D-glycero -D-galactonunulosaminic acid of formula (I).

USE - (I) is a known biologically active agent. It may now be used f' for treating disturbances of the nervous stimulus in the CNS and PNS especially for alterations in nervous transmissions at the CNS and PNS level; traumatic and toxic damage of the peripheral nerves; memory disturbances as a result of **Huntington**'s corea, senile dementia, confusion states of arteriosclerotic or vascular origin etc. For optical retrobulbar neurities, paralysis of the oculomotoric nerves, neuralgias of trigeminus, paralysis of the facial or Bell's nerve, Garcin's syndrome, Guillan Barre's syndrome, radiolites, diabetic and alcoholic polyneurites, obsterical paralysis, mononeuronical diseases, lateral amiotrophic sclerosis, myelopathic muscular atrophy, progressive bulbar paralysis, serious myasthenia, muscular dystrophy, and such disturbances as confused states, cerebral disturbances, cranial traumas, cerebrovascular

disturbances and thromboses. Dosage units for injection contain 0.025-0.5 weight% (I).
Dwg.0/0

ABEQ EP 120328 B UPAB: 19930925
Compsn. for treatment of states related to disturbances of the nervous stimulus in the CNS and PNS comprises **cytidine** monophosphate of 5-acetamido-3,5-dideoxy-D-glycero -D-galactonunulosaminic acid of formula (I).

USE - (I) is a known biologically active agent. It may now be used f for treating disturbances of the nervous stimulus in the CNS and PNS esp. for alterations in nervous transmissions at the CNS and PNS level; traumatic and toxic damage of the peripheral nerves; memory disturbances as a result of **Huntington**'s corea, senile dementia, confusion states of arteriosclerotic or vascular origin etc. For optical retrobulbar neuritis, paralysis of the oculomotoric nerves, neuralgias of trigeminus, paralysis of the facial or Bell's nerve, Garcin's syndrome, Guillan Barre's syndrome, radiolites, diabetic and alcoholic polyneurites, obstetrical paralysis, mononeuronical diseases, lateral amyotrophic sclerosis, myelopathic muscular atrophy, progressive bulbar paralysis, serious myasthenia, muscular dystrophy, and such disturbances as confused states, cerebral disturbances, cranial traumas, cerebrovascular disturbances and thromboses. Dosage units for injection contain 0.025-0.5 wt.% (I).
0/0

ABEQ US 4704361 A UPAB: 19930925
Prepn. of 5-acetylamino-3,5 -dideoxy-D-glycero-D-galactononulosaminic acid cytidine monophosphate (I) comprises condensn. of cytidine triphosphate (3-5 mmol) with N-acetylneuraminic acid (1 mmol) in the presence of cytidine monophosphate transferase (EC 2.7.7.43) and also a thiocarboxylic acid and a nitroimidazole as biological stabilisers (each 0.5-2 mmol per mmol cytidine triphosphate). The presence of these stabilisers gives much enhanced yields, e.g. 85%.$USE - The prods. (I) are therapeutics for pathological states arising from disturbances of the nervous stimulus in the central and peripheral nervous systems.

ABEQ US 5070079 A UPAB: 19930925
Compsns. contg. **cytidine** monophosphate of 5-acetamido-3,5-dideoxy-D-glycero-D-galactononulosamic acid (CMP-NANA) are used in the treatment of patients having brain lesions.

USE/ADVANTAGE - For the treatment of patients having brain lesions of the peripheral or central nervous system (claimed). Conditions treated include disturbances of the memory in the consequence of pathological events such as **Huntington**'s chorea, senile dementa, confusional states of arteriosclerotic or vascular origin, optical retrobulbar neurites, etc.

In an example, (I) is of low toxicity. LD50 values for albino rats where shown to be 900 mg/kg for intraperitoneal application, and 2400 mg/kg for the per os application.

L5 ANSWER 33 OF 55 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 1983-44742 DRUGU M B
TITLE: Antiviral Response of Fibroblasts from Familial Alzheimer's Disease and Down's Syndrome to Human Interferon-Alpha.
AUTHOR: Mowshowitz S L; Dawson G J; Elizan T S
LOCATION: New York, New York, United States
SOURCE: J.Neural Transm. (57, No. 1-2, 121-26, 1983) 1 Tab. 15 Ref.
CODEN: JNTMAH ISSN: 0300-9564
AVAIL. OF DOC.: Departments of Microbiology and Neurology, The Mount Sinai

School of Medicine of the City University of New York, New York, N.Y., U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 1983-44742 DRUGU M B
AB Antiviral sensitivity to human interferon-alpha was enhanced 5 fold in vesicular stomatitis virus (VSV) fibroblasts from Down's syndrome (T-21) patients, compared to normal (D-21) fibroblasts, and reduced in fibroblasts from 2/4 **Alzheimer**'s disease (AD) patients or relatives at risk. Functional association between T-21 and AD needs to be further investigated.
ABEX Fibroblast cell lines from 2 T-21 patients, 4 AD patients and 6 D -21 subjects (6-61 yr) were exposed to varying doses of interferon for 16 hr before infection with vesicular stomatitis virus (VSV) plus (3H) **uridine**. After 6 hr, VSV-specific RNA synthesis was measured. Relative sensitivity to cell lines was determined based on the reduction of VSV specific RNA synthesis in interferon treated cells. The sensitivity of GM276ZB T-21 cells was arbitrarily set at 10. Relative antiviral effects of interferon were 10-0.7 in T-21 fibroblasts, 1.0-4.5 in D-21 fibroblasts, 2.5-3.3 in 2 related AD fibroblast cell lines and 0.3 in 2 other related AD fibroblast cell lines.

L5 ANSWER 34 OF 55 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.
ACCESSION NUMBER: 1981:11090125 BIOTECHNO
TITLE: Differential labelling of UDP-N-acetylglucosamine in Huntington's-chorea fibroblasts
AUTHOR: Hung W.Y.; Tourian A.
CORPORATE SOURCE: Neurogenet. Cell Biol. Lab., Div. Neurol., Dept. Med., Duke Univ. Med Cent., Durham, N.C. 27710, United States.
SOURCE: Biochemical Journal, (1981), 196/2 (495-498)
CODEN: BIJOAK
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
AN 1981:11090125 BIOTECHNO
AB The hypothesis that there is impaired endogenous synthesis of glucosamine 6-phosphate in Huntington's-chorea fibroblasts was tested by double labelling matched pairs of fibroblasts in culture with carrier-free H.sub.3.sup.3.sup.2PO.sub.4 and ¢U-.sup.1.sup.4C!glucosamine. The ¢.sup.3.sup.2P!-UDP-N-acetyl¢.sup.1.sup.4C!glucosamine and ¢.sup.1.sup.4C!glucosamine 6-¢.sup.3.sup.2P!phosphate of the cellular soluble fraction was isolated by charcoal column and paper chromatography. There is no quantitative difference in .sup.3.sup.2P but a significant difference in .sup.1.sup.4C in these two sugars in a ratio of approx. 1.5 for Huntington's-chorea fibroblasts compared with normal fibroblasts.

L5 ANSWER 35 OF 55 FEDRIP COPYRIGHT 2003 NTIS
ACCESSION NUMBER: 2003:184933 FEDRIP
NUMBER OF REPORT: CRISP 5R01MH28783-25
RESEARCH TITLE: PSYCHOPHARMACOLOGICAL EFFECTS OF EXOGENOUS CHOLINE
STAFF: Principal Investigator: WURTMAN, RICHARD J; MASSACHUSETTS INST OF TECH, 77 MASSACHUSETTS AVE, CAMBRIDGE, MA 02139

PERFORMING ORGN: MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, MASSACHUSETTS
SUPPORTING ORGN: Supported By: NATIONAL INSTITUTE OF MENTAL HEALTH
FISCAL YEAR: 2001
FUNDING: Noncompeting Continuation (Type 5)
FILE SEGMENT: National Institutes of Health
SUM This application requests continued support for research on two families of chemicals in brain membranes - the phosphatides (e.g., phosphatidylcholine; PC) and amyloid-precursor protein (APP) - which may be involved in causing **Alzheimer**'s disease (AD). Research conducted in our laborato ry since this program's last competitive review (June, 1992) has shown, among other things, that the production of APP - like, as we previously showed, its conversion to non-amyloidogenic (i.e. presumably non-toxic) soluble forms - can be controlled by brain neurotransmitters (norepinephrine acting via beta receptors) and second messengers (cyclic AMP); that levels of **cytidine** in brain and in individual cells can limit the production of PC's immediate precursor, CDP-choline; that-as a consequence - CDP-choline can be used as a drug to treat strokes and memory impairment; and that when some cells are called upon to increase the rate at which they produce new membranes (e.g., neurite outgrowth in PC12 cells exposed to Nerve Growth Factor), the limiting factor in this process is a "second messenger", diacylglycerol (DAG) which in this circumstance acts as a bulk constituent. (The ability of orally- administered CDP-choline t o diminish stroke-induced neurological deficits has been demonstrated elsewhere in two large-scale "Phase III" studies, and a Now Drug Application [NDA] relating to this use will undergo evaluation by the FDA.) The new studies that we propose continue these lines of research, and relate to the synthesis, metabolism, and possible functions of APP; the sources of **cytidine** to the brain, and its interactions with choline and phospholipids; and the sources of the DAG needed to sustain neurite outgrowth. As before, we will attempt to apply our findings to the treatment of human diseases whenever possible.

L5 ANSWER 36 OF 55 INVESTEXT COPYRIGHT 2003 TFS

Accession No.: 1999:090791 INVESTEXT(tm) REPORT NUMBER:3367196
Page No.: PAGE 21 OF 33
Document No.: 3367196
Title: Swiss Pharmaceuticals
Author: Kulhoff, B.
Corp. Source: BANK SARASIN & CO.; SWITZERLAND
Region: WESTERN EUROPE REGION; EUROPE
Corp. So. Type: Financial center investment bank-broker
Publication Date: 1 Sep 1998
Report Type: INDUSTRY REPORT
File Segment: Text Page; INDUSTRY REPORT
Text Word Count: 248

L5 ANSWER 37 OF 55 INVESTEXT COPYRIGHT 2003 TFS

Accession No.: 1998:199451 INVESTEXT(tm) REPORT NUMBER:2600717
Page No.: PAGE 7 OF 17
Document No.: 2600717
Title: Roche - Company Report
Author: Hauber, A., et al
Corp. Source: SALOMON BROTHERS INC.; NEW YORK (STATE OF)

Region: MID-ATLANTIC/MIDDLE ATLANTIC REGION; UNITED STATES OF AMERICA; NORTH AMERICA
Corp. So. Type: Financial center investment bank-broker
Publication Date: 30 Oct 1997
Report Type: COMPANY REPORT
File Segment: Text Page; COMPANY REPORT
Text Word Count: 189

L5 ANSWER 38 OF 55 INVESTEXT COPYRIGHT 2003 TFS

Accession No.: 94:741646 INVESTEXT(tm) REPORT NUMBER:1464711
Page No.: PAGE 15 OF 57
Document No.: 1464711
Title: Biotechnology April 1994 Performance - Industry Report
Author: Miller, L.I., et al
Corp. Source: PAINEWEBBER INC.; NEW YORK (STATE OF)
Region: MID-ATLANTIC/MIDDLE ATLANTIC REGION; UNITED STATES OF AMERICA; NORTH AMERICA
Corp. So. Type: Financial center investment bank-broker
Publication Date: 19 May 1994
Report Type: INDUSTRY REPORT
File Segment: Text Page; INDUSTRY REPORT
Text Word Count: 460

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YOU HAVE REQUESTED DATA FROM FILE 'BABS, BIOTECHNO, CAPLUS, CONFSCI, FEDRIP, INVESTEXT, PASCAL, SCISEARCH, ADISCTI, ADISINSIGHT, BIOSIS, DGENE, DRUGU, LIFESCI, MEDLINE, PHAR, USPATFULL, WPIDS' - CONTINUE? (Y)/N:y

L5 ANSWER 41 OF 55 DGENE (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: AAW82500 Protein DGENE
TITLE: Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
INVENTOR: Hanover J A; Lubas W
PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES.
PATENT INFO: WO 9844123 A2 19981008 56p
APPLICATION INFO: WO 1998-US6101 19980327
PRIORITY INFO: US 1997-42270 19970331
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1998-557118 [47]
AN AAW82500 Protein DGENE
AB This sequence represents a novel human O-linked GlcNAc transferase, OGT protein (also known as **uridine** diphospho-N-acetylglucosamine: polypeptide beta -N-acetylglucosaminyl transferase). This protein is useful to assess predisposition toward type II diabetes in patients suspected of having hyperglycaemia that could evolve into this disease, by assaying OGT activity in red blood cells. It can also be used to assess predisposition toward **Alzheimer**'s disease, to assess the metastatic potential of tumours and to diagnose a tumour with metastatic potential. OGT can also be used to identify OGT inhibitors, especially in high-throughput assays, useful, e.g. in the treatment of diabetes

mellitus, tumour-derived diseases and **Alzheimer**'s disease.

L5 ANSWER 42 OF 55 DGENE (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: AAW82503 Protein DGENE
TITLE: Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
INVENTOR: Hanover J A; Lubas W
PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES.
PATENT INFO: WO 9844123 A2 19981008 56p
APPLICATION INFO: WO 1998-US6101 19980327
PRIORITY INFO: US 1997-42270 19970331
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1998-557118 [47]
AN AAW82503 Protein DGENE
AB This sequence is a rabbit OGT tryptic fragment. This sequence is used in the isolation of human and C. elegans OGT, O-linked GlcNAc transferase proteins (also known as **uridine** diphospho-N-acetylglucosamine: polypeptide beta -N-acetylglucosaminyl transferase). This protein is useful to assess predisposition toward type II diabetes in patients suspected of having hyperglycaemia that could evolve into this disease, by assaying OGT activity in red blood cells. It can also be used to assess predisposition toward **Alzheimer**'s disease, to assess the metastatic potential of tumours and to diagnose a tumour with metastatic potential. OGT can also be used to identify OGT inhibitors, especially in high-throughput assays, useful, e.g. in the treatment of diabetes mellitus, tumour-derived diseases and **Alzheimer**'s disease.

L5 ANSWER 43 OF 55 DGENE (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: AAW82502 Protein DGENE
TITLE: Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
INVENTOR: Hanover J A; Lubas W
PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES.
PATENT INFO: WO 9844123 A2 19981008 56p
APPLICATION INFO: WO 1998-US6101 19980327
PRIORITY INFO: US 1997-42270 19970331
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1998-557118 [47]
AN AAW82502 Protein DGENE
AB This sequence is a rabbit OGT tryptic fragment. This sequence is used in the isolation of human and C. elegans OGT, O-linked GlcNAc transferase proteins (also known as **uridine** diphospho-N-acetylglucosamine: polypeptide beta -N-acetylglucosaminyl transferase). This protein is useful to assess predisposition toward type II diabetes in patients suspected of having hyperglycaemia that could evolve into this disease, by assaying OGT activity in red blood cells. It can also be used to assess predisposition toward **Alzheimer**'s disease, to assess the metastatic potential of tumours and to diagnose a tumour with metastatic potential. OGT can also be used to identify OGT inhibitors, especially in high-throughput assays, useful, e.g. in the treatment of diabetes mellitus, tumour-derived diseases and **Alzheimer**'s disease.

L5 ANSWER 44 OF 55 DGENE (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: AAW82501 Protein DGENE
TITLE: Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
INVENTOR: Hanover J A; Lubas W
PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES.
PATENT INFO: WO 9844123 A2 19981008 56p
APPLICATION INFO: WO 1998-US6101 19980327
PRIORITY INFO: US 1997-42270 19970331
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1998-557118 [47]
AN AAW82501 Protein DGENE
AB This sequence represents a Caenorhabditis elegans OGT, O-linked GlcNAc transferase protein (also known as **uridine** diphospho-N-acetylglucosamine: polypeptide beta -N-acetylglucosaminyl transferase). This protein is useful to assess predisposition toward type II diabetes in patients suspected of having hyperglycaemia that could evolve into this disease, by assaying OGT activity in red blood cells. It can also be used to assess predisposition toward **Alzheimer**'s disease, to assess the metastatic potential of tumours and to diagnose a tumour with metastatic potential. OGT can also be used to identify OGT inhibitors, especially in high-throughput assays, useful, e.g. in the treatment of diabetes mellitus, tumour-derived diseases and **Alzheimer**'s disease.

L5 ANSWER 45 OF 55 DGENE (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: AAR79354 Protein DGENE
TITLE: Human double stranded ribonucleotide acid adenosine deaminase enzyme, DRADA - useful in treating neuro-degenerative disorder(s) e.g. Alzheimer's disease, etc.
INVENTOR: Nishikura K
PATENT ASSIGNEE: (WIST-N)WISTAR INST ANATOMY & BIOLOGY.
PATENT INFO: WO 9522604 A1 19950824 98p
APPLICATION INFO: WO 1995-US2275 19950216
PRIORITY INFO: US 1994-280443 19940725
US 1994-197794 19940217
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1995-302713 [39]
AN AAR79354 Protein DGENE
AB AAR79354 is a human double stranded ribonucleic acid adenosine deaminase enzyme (DRADA) C-terminal peptide which is believed to be a part of a multi-subunit enzyme complex which has a specific **cytidine** deaminase activity responsible for the RNA editing of apolipoprotein B mRNAs. The DRADA protein or fragments of the protein, polynucleotide sequence and DRADA antibodies are useful in the diagnosis of certain neurological or central nervous system disorders e.g. **Alzheimer**'s disease, Huntingdon's disease, subacute sclerosing panencephalitis (SSPE), measles inclusion body encephalitis, strokes, etc. The DRADA protein or protein fragments may be used to correct the malfunctioning of defects in glutamate-gated ion channels which result in **Alzheimer**'s disease, seizures or strokes.

L5 ANSWER 46 OF 55 DGENE (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: AAV69303 DNA DGENE
TITLE: Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
INVENTOR: Hanover J A; Lubas W
PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES.
PATENT INFO: WO 9844123 A2 19981008 56p
APPLICATION INFO: WO 1998-US6101 19980327
PRIORITY INFO: US 1997-42270 19970331
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1998-557118 [47]
AN AAV69303 DNA DGENE
AB This is a PCR primer used to amplify the C. elegans OGT, O-linked GlcNAc transferase protein (also known as **uridine** diphospho-N-acetylglucosamine: polypeptide beta -N-acetylglucosaminyl transferase). This protein is useful to assess predisposition toward type II diabetes in patients suspected of having hyperglycaemia that could evolve into this disease, by assaying OGT activity in red blood cells. It can also be used to assess predisposition toward **Alzheimer**'s disease, to assess the metastatic potential of tumours and to diagnose a tumour with metastatic potential. OGT can also be used to identify OGT inhibitors, especially in high-throughput assays, useful, e.g. in the treatment of diabetes mellitus, tumour-derived diseases and **Alzheimer**'s disease.

L5 ANSWER 47 OF 55 DGENE (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: AAV69304 DNA DGENE
TITLE: Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
INVENTOR: Hanover J A; Lubas W
PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES.
PATENT INFO: WO 9844123 A2 19981008 56p
APPLICATION INFO: WO 1998-US6101 19980327
PRIORITY INFO: US 1997-42270 19970331
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1998-557118 [47]
AN AAV69304 DNA DGENE
AB This is a PCR primer used to amplify the C. elegans OGT, O-linked GlcNAc transferase protein (also known as **uridine** diphospho-N-acetylglucosamine: polypeptide beta -N-acetylglucosaminyl transferase). This protein is useful to assess predisposition toward type II diabetes in patients suspected of having hyperglycaemia that could evolve into this disease, by assaying OGT activity in red blood cells. It can also be used to assess predisposition toward **Alzheimer**'s disease, to assess the metastatic potential of tumours and to diagnose a tumour with metastatic potential. OGT can also be used to identify OGT inhibitors, especially in high-throughput assays, useful, e.g. in the treatment of diabetes mellitus, tumour-derived diseases and **Alzheimer**'s disease.

L5 ANSWER 48 OF 55 DGENE (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: AAV69301 DNA DGENE
TITLE: Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
INVENTOR: Hanover J A; Lubas W
PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES.
PATENT INFO: WO 9844123 A2 19981008 56p
APPLICATION INFO: WO 1998-US6101 19980327
PRIORITY INFO: US 1997-42270 19970331
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1998-557118 [47]
AN AAV69301 DNA DGENE
AB This sequence encodes a novel human O-linked GlcNAc transferase, OGT protein (also known as **uridine** diphospho-N-acetylglucosamine: polypeptide beta -N-acetylglucosaminyl transferase). This protein is useful to assess predisposition toward type II diabetes in patients suspected of having hyperglycaemia that could evolve into this disease, by assaying OGT activity in red blood cells. It can also be used to assess predisposition toward **Alzheimer**'s disease, to assess the metastatic potential of tumours and to diagnose a tumour with metastatic potential. OGT can also be used to identify OGT inhibitors, especially in high-throughput assays, useful, e.g. in the treatment of diabetes mellitus, tumour-derived diseases and **Alzheimer**'s disease.

L5 ANSWER 49 OF 55 DGENE (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: AAV69306 DNA DGENE
TITLE: Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
INVENTOR: Hanover J A; Lubas W
PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES.
PATENT INFO: WO 9844123 A2 19981008 56p
APPLICATION INFO: WO 1998-US6101 19980327
PRIORITY INFO: US 1997-42270 19970331
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1998-557118 [47]
AN AAV69306 DNA DGENE
AB This is a PCR primer used to amplify the human OGT, O-linked GlcNAc transferase protein (also known as **uridine** diphospho-N-acetylglucosamine: polypeptide beta -N-acetylglucosaminyl transferase). This protein is useful to assess predisposition toward type II diabetes in patients suspected of having hyperglycaemia that could evolve into this disease, by assaying OGT activity in red blood cells. It can also be used to assess predisposition toward **Alzheimer**'s disease, to assess the metastatic potential of tumours and to diagnose a tumour with metastatic potential. OGT can also be used to identify OGT inhibitors, especially in high-throughput assays, useful, e.g. in the treatment of diabetes mellitus, tumour-derived diseases and **Alzheimer**'s disease.

L5 ANSWER 50 OF 55 DGENE (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: AAV69305 DNA DGENE
TITLE: Protein exhibiting O-linked GlcNAc transferase activity, OGT

- useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
INVENTOR: Hanover J A; Lubas W
PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES.
PATENT INFO: WO 9844123 A2 19981008 56p
APPLICATION INFO: WO 1998-US6101 19980327
PRIORITY INFO: US 1997-42270 19970331
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1998-557118 [47]
AN AAV69305 DNA DGENE
AB This is a PCR primer used to amplify the human OGT, O-linked GlcNAc transferase protein (also known as **uridine** diphospho-N-acetylglucosamine: polypeptide beta -N-acetylglucosaminyl transferase). This protein is useful to assess predisposition toward type II diabetes in patients suspected of having hyperglycaemia that could evolve into this disease, by assaying OGT activity in red blood cells. It can also be used to assess predisposition toward **Alzheimer**'s disease, to assess the metastatic potential of tumours and to diagnose a tumour with metastatic potential. OGT can also be used to identify OGT inhibitors, especially in high-throughput assays, useful, e.g. in the treatment of diabetes mellitus, tumour-derived diseases and **Alzheimer**'s disease.

L5 ANSWER 51 OF 55 DGENE (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: AAV69302 DNA DGENE
TITLE: Protein exhibiting O-linked GlcNAc transferase activity, OGT - useful, e.g. to assess predisposition to type II diabetes or Alzheimer's or metastatic potential of tumours, and to identify inhibitors
INVENTOR: Hanover J A; Lubas W
PATENT ASSIGNEE: (USSH)US DEPT HEALTH & HUMAN SERVICES.
PATENT INFO: WO 9844123 A2 19981008 56p
APPLICATION INFO: WO 1998-US6101 19980327
PRIORITY INFO: US 1997-42270 19970331
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1998-557118 [47]
AN AAV69302 DNA DGENE
AB This sequence encodes a novel Caenorhabditis elegans OGT, O-linked GlcNAc transferase protein (also known as **uridine** diphospho-N-acetylglucosamine: polypeptide beta -N-acetylglucosaminyl transferase). This protein is useful to assess predisposition toward type II diabetes in patients suspected of having hyperglycaemia that could evolve into this disease, by assaying OGT activity in red blood cells. It can also be used to assess predisposition toward **Alzheimer**'s disease, to assess the metastatic potential of tumours and to diagnose a tumour with metastatic potential. OGT can also be used to identify OGT inhibitors, especially in high-throughput assays, useful, e.g. in the treatment of diabetes mellitus, tumour-derived diseases and **Alzheimer**'s disease.

L5 ANSWER 52 OF 55 PHAR COPYRIGHT 2003 PJB
TX Wellstat Therapeutics (Wellstat) is developing triacetyluridine (PN-401), a po prodrug of the nucleoside, **uridine**, to enable higher dosage of 5-FU to be administered to cancer patients.

It is also under development for the treatment of various neurodegenerative disorders associated with **mitochondrial dysfunction**. Its mechanism of action is unknown.

Clinical

Phase IIIIt is in a randomized, open-label Phase III trial in N America in 260 stage II-IV pancreatic cancer patients. Patients will receive PN-401 po once-daily x2 days in combination with either 5-FU iv 1x/wk x3 with 1wk rest for a 4wk cycle or gemcitabine hydrochloride (qv) iv 1x/wk x7 with 1wk rest for a 4wk cycle.

Phase IIIt is in a Phase II trial (S9915) in combination with 5-FU and leucovorin in unresectable or metastatic adenocarcinoma of the stomach.

Phase IIt is in Phase I trials for the treatment of colorectal cancer and neurodegenerative diseases (Company Web Page, Wellstat, Nov 2002).

Preclinical
It has shown efficacy in murine models of Alzheimer's, Huntington's and Parkinson's diseases and in models of peripheral neuropathy. PN-401 was neuroprotective against chemically-induced hypoxia and H2O2 toxicity (32nd Meet Soc Neurosci (Orlando), 2002, Abs 322.4 and 685.15). Entered by KK on 12/11/2002.

L5 ANSWER 53 OF 55 PHAR COPYRIGHT 2003 PJB
TX Triacetyluridine (RG-2133) is a prodrug of **uridine** under development by RepliGen for the treatment of bipolar disorder, major depression, renal tubular acidosis and **mitochondrial disease**.

Marketing
RepliGen has licensed from the University of California, San Diego (UCSD), CA, the US, 2 patents covering the use of **uridine** for the treatment of **mitochondrial diseases** and purine autism. RepliGen has exclusive commerical rights in exchange for upfront, milestone and royalty payments (Press releases, RepliGen, 5 Mar 2001 and 23 Jan 2003; Ann Rep, RepliGen, 2002). It has US orphan drug status for use in **mitochondrial disease**.

Clinical

Phase IIIt is in a 4wk dose-escalation, open-label US Phase I/II trial in 12 patients with mitochondrial disease. RG-2133 tolerance will be evaluated, as well as its impact on symptoms including renal function, seizures or cardiac function (Press release, RepliGen, 13 Feb 2003). An open-label US Phase I/II safety and efficacy trial has also been initiated. The trial will assess the impact of RG-2133 on depressive symptoms, and will evaluate potential changes in brain chemistry by magnetic resonance spectroscopy in 20 patients before and after 6wk of treatment with RG-2133 po (Press release, RepliGen,

23 Jan 2003).

Phase IIn a Phase I trial in 15 **mitochondrial disease** patients (including children), **uridine** po or TAU produced improvements in cognitive and muscular function over 2yr, and was well tolerated (Press release, RepliGen, 14 Dec 2000; Ann Rep, RepliGen, 2002). In 4 patients with renal tubular acidosis, **uridine** or TAU produced a rapid improvement or correction of kidney function (Press release, RepliGen, 5 Mar 2001).

Preclinical
Uridine was active in a well-validated animal model of depression (Press release, RepliGen, 23 Jan 2003). Updated by WB on 17/2/2003.

L5 ANSWER 54 OF 55 BABS COPYRIGHT 2003 BEILSTEIN CDS MDLI
ACCESSION NUMBER: 6178733 BABS
TITLE: Metabolism and Actions of CDP-Choline as an Endogenous Compound and Administered Exogenously as Citicoline
AUTHOR(S): Weiss, George B.
SOURCE: Life Sci. (1995), 56(9), 637 - 660
CODEN: LIFSAK
DOCUMENT TYPE: Journal
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 6178733 BABS
AB CDP-choline, supplied exogenously as citicoline, has beneficial physiological actions on cellular function that have been extensively studied and characterized in numerous model systems. As the product of the rate-limiting step in the synthesis of phosphatidylcholine from choline, CDP-choline and its hydrolysis products (**cytidine** and choline) play important roles in generation of phospholipids involved in membrane formation and repair. They also contribute to such critical metabolic functions as formation of nucleic acids, proteins, and acetylcholine. Orally-administered citicoline is hydrolyzed in the intestine, absorbed rapidly as choline and **cytidine**, resynthesized in liver and other tissues, and subsequently mobilized in CDP-choline synthetic pathways. Citicoline is efficiently utilized in brain cells for membrane lipid synthesis where it not only increases phospholipid synthesis but also inhibits phospholipid degradation. Exogenously administered citicoline prevents, reduces, or reverses effects of ischemia and/or hypoxia in most animal and cellular models studied, and acts in head trauma models to decrease and limit nerve cell membrane damage, restore intracellular regulatory enzyme sensitivity and function, and limit edema. Thus, considerable accumulated evidence supports use of citicoline to enhance membrane maintenance, membrane repair, and neural function in conditions such as ischemic and traumatic injuries. Beneficial effects of exogenous citicoline also have been postulated and/or reported in experimental models for dyskinesia, Parkinson's disease, cardiovascular disease, aging, **Alzheimer**'s disease, learning and memory, and cholinergic stimulation.

L5 ANSWER 55 OF 55 CONFSCI COPYRIGHT 2003 CSA
ACCESSION NUMBER: 91:28743 CONFSCI
DOCUMENT NUMBER: 91057540
TITLE: RNA coding for the **Alzheimer** amyloid precursor protein interacts in vitro with the adenosine-**uridine** binding factor

AUTHOR: Malter, J.; Miller, D.L.; Denman, R.
CORPORATE SOURCE: Tulane Univ. Sch. Med.
SOURCE: FASEB, 9650 Rockville Pike, Bethesda, MD 20814, USA, Abstracts, FASEB Journal.
Meeting Info.: 912 0204: 75th Annual Meeting of FASEB (9120204). Atlanta, GA (USA). 21-25 Apr 1991. Federation of American Societies for Experimental Biology.
DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: UNAVAILABLE